PERIODONTAL REGENERATION OF 1-, 2-, AND 3-WALLED INTRABONY DEFECTS USING ACCELL CONNEXUS® VERSUS DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT: A RANDOMIZED PARALLEL ARM CLINICAL CONTROL TRIAL

by

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CERTIFICATE OF APPROVAL

MASTER'S THESIS

This is to certify that the Master's thesis of

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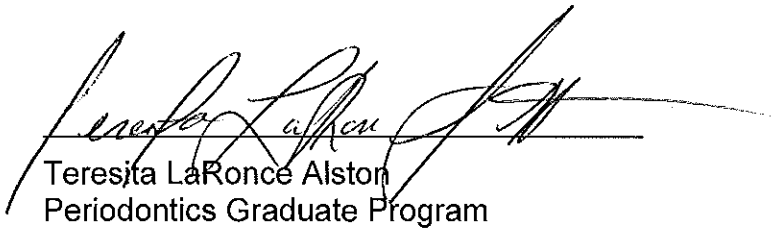

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ABSTRACT

PERIODONTAL REGENERATION OF 1-, 2-, AND 3-WALLED INTRABONY DEFECTS USING ACCELL CONNEXUS VERSUS® DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT: A RANDOMIZED PARALLEL ARM CLINICAL CONTROL TRIAL

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Introduction: Combination therapy, in guided tissue regeneration (GTR), is often used in the treatment of intrabony defects. Particulate demineralized freeze- dried bone allograft (DFDBA) is a bone grafting materials used successfully in GTR on humans for almost 30 years. A newer form of DFDBA, Accell Connexus® (Accell), has been FDA approved for use in periodontal regeneration which is the growth of new bone, cementum and periodontal ligament on a previously diseased tooth root surface. Accell Connexus® contains 5-7 times more bone morphogenic proteins (BMP) than the traditional particulate DFDBA. This increase in BMP is thought to increase the potential of periodontal regeneration.

Methods: A total of 30 patients diagnosed with severe periodontitis having an intrabony defect with a probing depth of $\geq$ 6 mm are included in this study. Customized plastic stents were fabricated to obtain standardized clinical probing depth (PD) and clinical attachment level of the defects at baseline, surgery, 6 and 12 months post-surgery. Standardized digital radiographs were taken using a customized bite-plate and a paralleling device for reproducibility of periapical radiographs at baseline and at 6 and 12 months after surgery. All participants received the same standardized surgical approach for GTR combination therapy. After defect debridement, and before root surface treatment with ethylenediaminetetraacetic acid (EDTA), the surgical team opened the sealed envelope containing the name of the bone graft material randomized to the participant's study number: DFDBA (control) or Accell (test). Fifteen patients will receive DFDBA and 15 patients Accell. Participants were re-evaluated to assess postoperative healing at weeks 1, 2, 4, 6, 8, 12, and 16, and again at 6, 9 and 12 months. After the 12 month re-evaluation, participants continued periodontal maintenance therapy with their providers. This interim data analysis compared changes in plaque index, bleeding on probing, PD, CAL and radiographic bone levels at baseline, 6 and 12 months post-surgery using the Mann-Whitney U test.

Results: A total of 21 subjects have been enrolled in this study and surgery has been completed on 20. Six month results have been finalized on 14 subjects and 1 year results on 13 of the subjects. Three patients were exited. Two of the exited patients were from the Accell group and 1 from the DFDBA group. At this time there were 13 complete sets of data therefore 13 sets of 6 month and 1 year results were analyzed with 8 subjects in the DFDBA group and 5 in the Accell group for this interim analysis. No significant difference was found with respect to bleeding on probing (BOP) or plaque scores. The mean probing depth (PD) decreased from 7.6 to 3.8mm for Accell and from 8mm to 4mm for DFDBA. Mean gain of CAL was 3.4mm for Accell and 3.0mm for DFDBA. Accell and DFDBA attained positive percent radiographic bone fill; 65.79% and 59.9% respectively. The results were not statically significant.

Discussion: Definitive conclusions cannot be drawn at this time because 12 month clinical measurements have been made in less than half of the subjects in the approved sample size.

Conclusions: The data analysis at this point does not show any significant statistical difference in clinical and radiographic outcomes between DFDBA and Accell. Both bone graft materials resulted in improved clinical parameters.

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LIST OF ABBREVIATIONS

GTR	Guided Tissue Regeneration
BMP	Bone Morphogenetic Protein(s)
BOP	Bleeding on Probing
OHI	Oral Hygiene Instructions
SRP	Scaling and Root Planning
OFD	Open Flap Debridement
CAL	Clinical Attachment Level
CEJ	Cementoenamel Junction
DFDBA	Demineralized Freeze-Dried Bone Allograft
EDTA	Ethylenediaminetetraacetic acid
FDBA	Freeze-Dried Bone Allograft
GS	Gingival Sulcus
JE	Junctional Epithelium
CO	Supracrestal Fibers
AC	Alveolar Crest
OE	Oral Epithelium
PD	Probing Depth
PDL	Periodontal Ligament
SE	Sulcular Epithelium
SEM	Scanning Electron Microscope
HCG	Human Chorion Gonadotropin
NPDS	Naval Postgraduate Dental School

CHAPTER I: INTRODUCTION

According to the 4th Edition of the Glossary of Periodontal terms, periodontal regeneration is the "reproduction or reconstitution of a lost or injured part" related to a diseased periodontium. The periodontium consist of the periodontal ligament, cementum and bone that surround the tooth. When these structures are destroyed due to periodontal disease the bone is lost creating a horizontal defect (flat) or a vertical intrabony defect. The potential to regenerate them is termed guided tissue regeneration (GTR). Completing GTR for regeneration of an intrabony defect is more predictable than for a horizontal defect. Over the years many specific techniques have been utilized however one GTR technique is to employ the use of a barrier membrane with a bone graft after the defect has been debrided and the root surface properly cleaned.

The purpose of the membrane is to allow for selective cell exclusion (Melcher, 1976). This means to prevent faster growing cells like the epithelium and connective tissue or collectively termed the gingival corium from rapidly growing into the site where slower growing cells; the periodontal ligament (PDL) fibroblast, cementoblast and osteoblast, would normally populate. This exclusion would allow for regeneration of the lost parts of the periodontium. Two main types of barrier membranes exist resorbable and non-resorbable. Resorbable collagen membranes prevent the need for a second surgical procedure which must be done to remove a non-resorbable membrane.

Although bone grafts are not always used in GTR procedures it has been shown that the addition of a bone graft can enhance regeneration (Bowers 1989 a, b, c). There are several types of bone grafting materials however the use of demineralized freeze dried bone allograft (DFDBA) was the first type of bone graft material to histologically

demonstrate regeneration (Bowers 1989 b, c) and is considered the gold standard for GTR with bone grafts. Newer forms of DFDBA have been formulated to include Accell Connexus®, which is believed to increase the potential of regeneration due to its ability to stay in place and its increased amount of bone morphgenic proteins (BMP).

If the combination of a membrane and a bone graft can enhance periodontial regeneration; will the combination of a non-resorbable membrane and a newer form of DFDBA, Accell Connexus®, further enhance periodontal regeneration?

Chapter II: Review of the Literature
Overview

Techniques for the surgical treatment of intrabony defects has varied from; open flap debridement, gingivectomy, osseous therapy, guided tissue regeneration (GTR), GTR with bone graft, GTR with bone graft and membrane, laser therapy to extraction of the tooth. Although completing a simple gingivectomy to address an intrabony lesion is no longer an accepted standard of care (Schluger, 1949) all of the other surgical options are still utilized as a standard form of care for intrabony defects. Of those treatment options GTR has been employed since the early 1980's. The concept of periodontal GTR was first described in humans by Dr. Sture Nyman and colleges who found that a new connective tissue attachment could form on a previously diseased root surface (Nyman, 1982). They tested a single severe, chronic infected mandibular incisor having a clinical attachment level of 11mm and a 2mm intrabony component at which point a crestal level notch was made in the tooth. After degranulation along with scaling and root planning a Millipore filter non-resorbable membrane was properly sized to cover an area coronal to the cemental enamel junction (CEJ) to slightly beyond the bony crest. The site was sutured with the membrane slightly exposed and was allowed to heal for three months. Histologically, they found collagen fibers inserting into newly formed cementum 5mm beyond the notch and bone regenerated only to the level of the bony crest. This proved that regeneration could occur on a previously diseased root surface.

In the field of periodontics it is import to regenerate bone, cementum and the periodontal ligament (PDL) that have been lost around teeth due periodontitis. The bone, cementum and PDL are also known as the periodontal attachment or periodontium. When reconstituting these parts the process of GTR can be utilized. GTR is a procedure attempting to restore lost periodontal structures through differential tissue responses (Melcher, 1976). The

use of barrier techniques, using membranes such as polytetrafluoroethylene, expanded polytetrafluoroethylene (ePTFE), polyglactin, polylactic acid, calcium sulfate and collagen, are employed in the hope of excluding epithelium and the gingival corium from the root or existing bone surface in the belief that they interfere with regeneration. Along with membranes, bone substitutes can also be applicable in GTR. The use of both a membrane and bone grafts together is termed combination therapy. Bone replacement grafts such as autografts, allograft, isografts, xenografts and alloplast have been used (Bowers, 1989b; Bowers, 1989c; Reynolds, 2003). In addition growth factors like; transforming growth (TGF), insulin like growth factor (IGF), vascular endothelial growth factor (VEG-F), enamel matrix derivative (EMX) and platelet derived growth factor (PDGF) have been used to assist in periodontal regeneration(Giannobile 2003; Marx 2004; Chong 2006). Some clinicians apply conditioners to prepare the root surface for GTR with hopes that a chemically cleaner root surface would assist in gaining additional new periodontal attachment beyond that of scaling root planning alone (Lafferty 1993.)

The following review of the literature will address periodontitis and periodontal regeneration as it relates to 1-, 2-, and 3-walled intrabony defects utilizing the GTR technique with and without bone grafts. This literature review will also seek to find a possible difference in percentage of regenerated periodontium with Accell Connexus®, a second generation demineralized freeze-dried bone allograft product that contains 5-7 times the amount of bone morphogenetic proteins (BMP) as regular demineralized freeze-dried bone allograft (DFDBA) and compare it to traditional particulate DFDBA while employing a porcine collagen membrane, Bio-Gide, as an exclusion barrier.

The Periodontium

The periodontium [(periodontal attachment and the gingival tissue (gums)] refers to the tissues that support teeth in the alveolus of the maxilla and the mandible (jaws). The periodontium consists of gingiva, PDL, cementum and bone. The cementum surrounds the root surface and is attached to the alveolar housing (tooth socket) via the PDL which suspends the tooth within the alveolus. The gingival tissue is composed of epithelium (oral, sucular and junctional) and supracrestal connective tissue fibers located coronal to the level of the bone and PDL. The epithelial-lined sulcus or crevice encircles teeth while the junctional epithelium forms a hemidesomal attachment to the tooth surface (Pöllänen, Salonen, & Uitto, 2000). The gingival soft tissue also consist of gingival fibers that surrounds the tooth to assist in attaching the gingival tissue to the cementum, holding the gingival tissues firmly against the tooth and preventing deflection of the gingival tissue during mastication (Hassel, 1993).

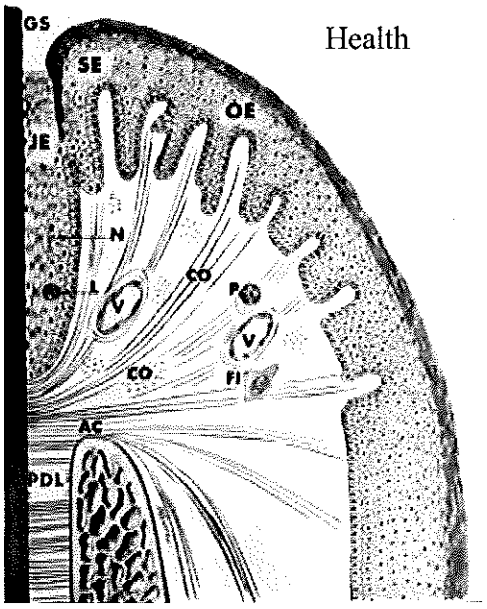

Figure 1. The Periodontium in Health. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Page and Schroeder's Model of Pathogenesis (1976) with images for health, gingivitis and periodontitis (Figures 1, 2 and 3) is the illustrator's model of health and disease. Three types of epithelial tissues characterize the gingiva (see figure 1) : (1) the keratinized oral epithelium (OE) that comprises the visible band of gingiva around the teeth, (2) the sulcular epithelium (SE), which is the transition tissue at the edge of the tooth, and (3) the specialized non-keratinized epithelium called the junctional epithelium (JE) that lines the bottom of the gingival sulcus (GS). The JE is attached to the tooth via hemidesmosomes which are made of adhesion proteins called integrins. In health (Figure 1) the JE is the first barrier to prevent bacterial plaque from reaching the underlying connective tissue and bone. The terms gingival sulcus (GS) and gingival crevice are used interchangeably. Also in figure, 1 the image depicting "Health" shows how the intact JE, supracrestal fibers (CO) and the PDL between the alveolar bone and root surface support a tooth. The PDL fibers serve as the connective tissue support that holds the tooth in place in the bone and helps cushion the tooth from forces when we bite, chew or clench (Beertsen, McCulloch, & Sodek, 2000). The PDL contains pressure receptors that are activated by tooth contact. The impulses generated by these receptors are sent to the brain and used to help coordinate the sequencing of jaw movement (Byers & Dong, 1989).

The Periodontium in Disease

Gingival inflammation or gingivitis is caused by bacterial plaque that when allowed to remain in the GS for an extended period of time will cause a degree of inflammation within the gingival tissues. The amount of time to develop gingivitis

depends on the individual however the average range is 10- 21 days (Loe, Theilade & Jensen, 1965). As seen in Page and Schroeder's "Gingivitis" diagram (Figure 2), the integrity of JE is disturbed when inflammatory cells accumulate in the underlying connective tissue. In gingivitis, the early form of periodontal disease, the gingival tissue may become red, swollen and tender and often bleeds on manipulation i.e. brushing, flossing and probing. While the supracrestal gingival fibers can become irritated, the PDL attachment and the alveolar bone remain intact.

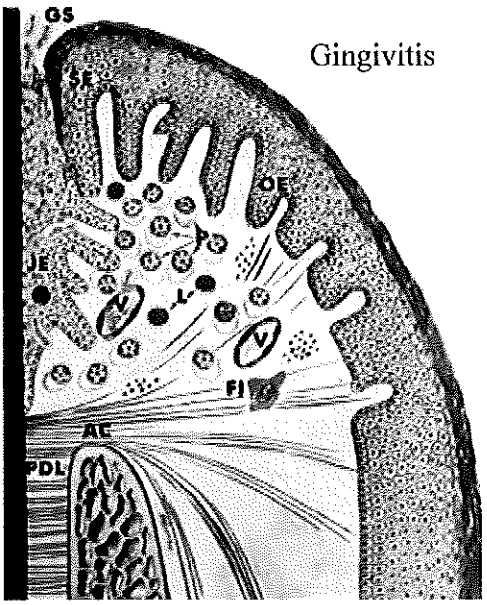

Figure 2. The periodntium with gingivitis. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Gingivitis transitions to periodontitis when the host's immune response cannot resist bacterial plaque and the inflammatory process (Weinman, 1941; Takata & Donath, 1988). Destruction of connective tissue and alveolar bone, leading to possible tooth loss, is a consequence of the interaction between the plaque front and immune response (Waerhaug 1977; Haffajee, Socransky & Goodson, 1983). This tissue breakdown is clear in Page and Schroeder's "Periodontitis" diagram (Figure 3). With the onset of periodontitis, the gingival crevice becomes a deeper periodontal pocket,

with destruction of supracrestal gingival fibers, PDL, and the breakdown of the alveolar bone. This process of connective tissue and bone destruction is called clinical attachment loss.

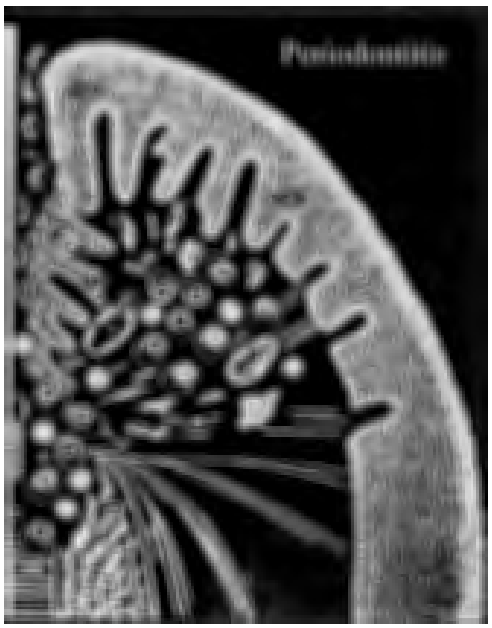

Figure 3. The periodntium with periodontitis. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Clinical attachment loss is a measure of how much periodontal support has been destroyed. It is assessed by gently inserting a periodontal probe into the GS or a periodontal pocket to measure the distance from the CEJ to the base of the periodontal pocket. The University of North Carolina (UNC) 15 periodontal probe has 1 mm increments with color coding at the fifth, tenth and fifteenth millimeter. In health, insertion of the periodontal probe is resisted by the intact connective tissue and probing depths should measure 3 mm or less. When periodontal disease is present, the periodontal probe inserts more deeply into the pocket because the connective tissue has been destroyed (Fowler, Garrett, Crigger & Engelberg, 1982). In a diseased state, the probing depths will be 4 mm or greater, and the tissue may bleed upon probing

(Armitage, Svanberg & Loe, 1977). Probing depth measurements aid in the diagnosis of the severity of periodontal disease. It is not uncommon to have healthy and significantly diseased locations within the same person and on the same tooth (Haffajee & Socransky, 1986).

As the disease process continues and more connective tissue is lost, bone loss becomes evident on radiographs. Once sufficient mineral content in the bone has been destroyed (Bender, 1961). The radiograph provides a visual tool for detecting and characterizing intrabony defects (Rees, 1971). However, clinical detection of attachment loss, indicated by deeper probing depths, usually precedes radiographic evidence of bone loss by a period of six to eight months (Goodson, Haffajee & Socransky, 1984). Probing depths, clinical attachment level (CAL), and radiographs help clinicians assess extent (localized or generalized), duration (chronic or aggressive) and severity (mild, moderate or severe) of periodontal disease which will assist in rendering the appropriate treatment. Radiographs assist in determining whether bone loss is horizontal, vertical, or a combination of the two. A normal bony pattern is shown in figure 4a. Horizontal defects appear on radiographs as bone that has decreased in a parallel manner to the occlusal table (Figure 4b). Whereas in vertical defects, the bone is lost in a mode that depicts an intrabony defect or a defect which appears to have a wall or multiple walls surrounding a defects (Figure 4c). Although horizontal bone loss is often associated with slowly progressing disease both horizontal and intrabony defects can be seen in chronic forms of periodontal disease.

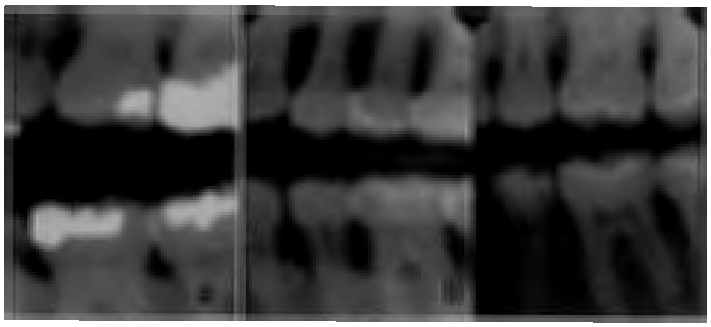

Figure 4a shows a normal bony pattern in which the bone level follows the cemental enamel junction (CEJ) with no clinical loss of bone.
Figure 4b shows horizontal bone loss where the bone appears to recede away from the CEJ evenly.
Figure 4c shows vertical bone loss on the mesial and distal of #14. Note that the bone appears to have lost a wall buccal or lingually.
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Combination defects are sometimes difficult to see radiographiclly. However a combination defect can be seen in figure 4c on the mesial of #14. Note that the tooth has lost bone in a vertical configuration however the mesial of #14 also radiographiclly presents with a difference in color contrast. The difference in contract may be a combination 1, 2, or 3 wall vertical, intrabony, defect. However one can only make an assumption using radiographs as to the type of vertical defect because vertical defects are better visualized surgically and can often be missed radiographiclly if they are less than 3mm (Paul and Trott, 1966). Below is a surgically exposed example of a 3 walled intrabony defect on a mandibular second molar.

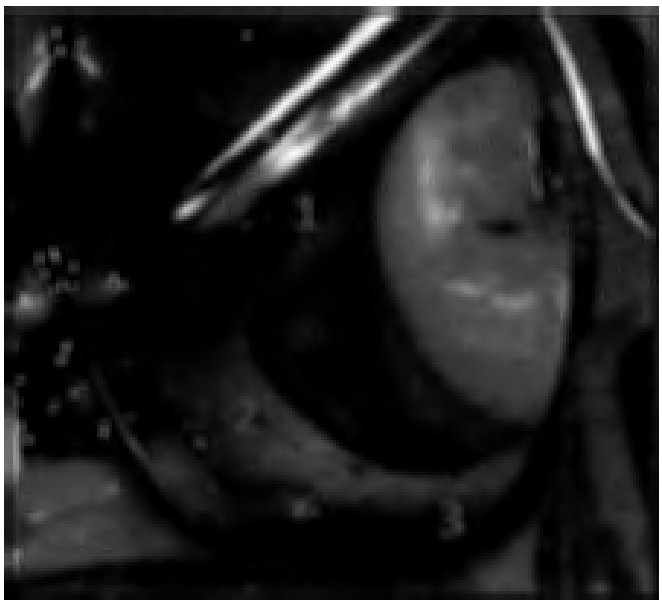


Figure 5. This depicts a three walled defect. Used with permission from the author of this thesis, LCDR Teresita Alston.

The Etiology of Periodontitis

The prerequisite for developing periodontitis is gingivitis, which develops within 1-3 weeks of bacterial plaque contact with the gingival tissues (Löe, Theilade, Jensen, 1965). Although gingivitis is a must to progress to periodontitis not all individuals who develop gingivitis will progress to periodontitis. In fact, the etiology of bone loss in periodontics is due to bacterial plaque in a susceptible host (Waerhaug, 1977; Page, 1992). One can become prone to periodontitis due to systemic diseases, genetics, local factors (calculus, poorly placed restorations, tooth anatomy, root fractures), oral infections (Armitage, 1999), smoking (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993; Tomar& Asma, 2000) or viruses, (Contreras & Slots, 2000).

The local factor, calculus, is often seen in individuals with periodontitis and calculus can assist in further destruction of bone. Within the oral cavity calculus is covered by a layer of plaque which may contain a variety of bacteria both non-pathogenic and pathogenic (Socransky, Haffajee, & Smith, 1998). Although living bacteria can be harmful it has been demonstrated in an animal model that even sterile calculus can cause a foreign body reaction (Allen & Kerr, 1965). This showed that calculus, even sterile, can cause an issue within an otherwise healthy environment. Although we know calculus can cause a reaction it is sometimes difficult to detect clinically and on radiographs. It has been shown that radiographs have a low sensitivity and a high specificity and that the detection of calculus is subjective to its thickness (Buchananan, Jenderseck, Granet, Kircos, Chambers & Robeertson, 1987). Even though calculus at times may be difficult to detect it should be removed to prevent destruction or lessen the severity of the destruction.

The level of destruction is often dependent on the type if bacterial microflora involved. The bacterial microflora exists in complexes in subgingival plaque and has been divided into five major color coded complexes (Socransky, Haffajee, & Smith, 1998). Not all complexes are associated with periodontitis however the more virulent bacteria are found in the red complex. According to Socransky, 1998 the gram negative red complex which consist of *Bacteroides forsythus, Porphyromonas gingivalis* and *Treponema denticola* are highly related to increase pocket depth and bleeding on probing. *Aggregatibacter actinomycetemcomitans,* formally, *Actinobacillus*, is found within the green complex however multiple serotypes exist (Yang, 2004). However one serotype, serotype b, though it may cause destructive periodontal disease is not within

the green spectrum. Orange complex bacteria, *Fusobacterium nucleatum, Prevotella intermedia, Prevotella nigrescens and Peptostreptococcus micros*, have also been shown populate diseased sites. Those gram negative bacteria as well as others have been found to be associated with active periodontal lesions (Kornman, 1986). Again not all gram negative bacteria are associated with active periodontal disease. In several studies, *Bacieroides intermedius.* "fusiform" *Bacteroides. Actinobacitlus aeiinomyeetemeoniitans* and *Woiinella recia. Fusobacterium nucleatum. Capnoeyiophaga gingivalis* and *Eikenella corrodens* were found in higher numbers in non-active sites (Dzink, Tanner, Haffajee & Socransky, 1985).

Smoking and Periodontitis

Smoking can increase ones risk of developing more severe periodontal disease (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993). In fact it is believed that smokers account for 41.9% of periodontitis cases and former smokers account for another 10.9% of periodontitis (Tomar& Asma, 2000). In the NHANES study conducted between 1988 and 1994 found that 27.9% of the U.S. populations are smokers and 23.3% are former smokers (Tomar& Asma, 2000). Smoking can increase ones risk of developing more severe periodontal disease more rapidly (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993; Stoltenberg, Osborn, Pihlstrom, Herzberg, Aeppli, Wolff & Fischer, 1993; Tomar& Asma, 2000). Even in those with very low levels of plaque increase their risk. According to the AAP 1999 position paper when plaque levels were adjusted for in several studies, smokers had greater probing depths, clinical attachment loss and bone loss. Bergstrom, Eliasson and Preber, 1991 completed a

study with Swedish dental hygienist and found that smokers had 1.71mm of bone loss compared to 1.45mm in non-smokers. This demonstrated that even in the presence of good oral hygiene smoking leads to greater loss of attachment.

When studying the bacteria found in the pockets of those who smoked, one study found that smokers have a greater extent of colonization of red and orange complex bacteria in pocket depths less than 4 mm (Haffajee & Socransky, 2001) however other studies determined that there was no significant difference in any combination of bacteria when they compared smokers to non-smokers (Bergstrom, Linder,1992; Stoltenberg, Osborn, Pihlstrom, Herzberg, Aeppli, Wolff, Fischer, 1993). Nevertheless there was a difference in treatment outcome when it came to treating smokers who had periodontial disease. In a studying comparing heavy smokers (more than 19 cigarettes per day) to light smokers (less than 19 cigarettes per day), former smokers and never smokers, smokers responded less favorable to periodontal therapy (Ah, Johnson, Kaldahl, Patil & Kalkwarf, 1994; Kaldahl, Johnson, Patil, Kalkwarf, 1996). Although less favorable smokers did respond positively to treatment (Kaldahl, Johnson, Patil, Kalkwarf, 1996; Rosen, Marks, Renolds, 1996). Preber and Bergstrom (1986) attained a slight difference in probing depth reduction 1.1mm in smokers and 1.2mm in non-smokers in probing depths of 4-6mm with non-surgical therapy. When periodontal regenerative therapy using DFDBA in 110 intrabony lesions was carried out and followed for 1, 2 and 5 years it was noted that both smokers and non-smokers had an improvement in clinical attachment levels (2.7mm : 3.4mm), plaque score, and probing depths (3.0mm : 3.8mm) at one year post surgery. However smokers had significantly inferior CAL gain (smokers 29.2%: non-smokers 42.5%) when compared to

pretreatment parameters at 1, 2 and 5 years post-surgery (Rosen, Marks, Reynolds, 1996). However if smokers stopped smoking they may experience the same healing as those who never smoked (Grossi, Zambon, Machtei, Schifferle, Andeeana, Genco, Cummins & Harrap, 1997).

Although bone loss can become more severe due to certain systemic diseases, necrotizing disease, periodontial abscess, combination endodontic/ periodontic lesions or developmental/ acquired deformities (Armitage, 1999) this literature review will not cover those topics.

Treatment of Periodontitis

All periodontal patients should have a review of their medical history; head and neck exam; full mouth periodontal examination and a full mouth series of radiographs or a comparable radiographic assessment. A full mouth periodontal examination should record a minimum of PD, CAL, BOP, recession (amount of root seen clinically), furcation involvement, purulence, plaque and mobility. After the review of the medical history; the complete periodontal evaluation and review of radiographs a diagnosis can be made. Schallhorn published an article in 1977 that presented a flow for the treatment osseous defects however can be applied to other treatment. The author pointed out that once the diagnosis has been formulated the first phase of periodontal treatment can take place followed by different ways to proceed to the next phase or move among the phases of periodontal treatment. In the first phase, the patient would receive palliative care; extraction of hopeless teeth due to periodontal reasons or otherwise; oral hygiene instructions (OHI) on the proper techniques of oral hygiene

along with initial therapy; and any other procedure the clinician believes must be taken care of prior to re-evaluation. Initial therapy consists of removal the plaque and calculus accumulation both supra and subgingivally non-surgically. The removal of accretions from the root along with diseased cememtum is called scaling and root planning (SRP). Many people refer to this as a deep cleaning. Although this is call a deep cleaning the effectiveness of SRP decreases as the pocket depth becomes deeper. Stambaugh (1981) found that a PD beyond 3.73mm the efficacy of SRP is less. That study confirmed a previous study conducted on teeth that underwent SRP, by experienced hygienist, on teeth at various PD then extracted them to see the effectiveness of SRP. The study found that the deeper the site the greater the percentage of deposits are left on the root. In fact, a PD greater than 3mm left calculus behind 17% of the time; PD between 3-5mm calculus was left behind 61% of the time and PD greater than 5mm calculus was behind 89% of the time (Waerhaug, 1978). Therefore the predictability of effectively cleaning PD greater than 4mm is greatly decreased with non-surgical therapy. After a period of 4-6 weeks patients are re-evaluated to assess their response to initial therapy (Proye, 1982). If the patient has residual areas of deep probing depths (>4mm) with signs of inflammation like BOP then the clinician may decide that surgical corrective therapy may be the best option for the patient.

The goal of non-surgical periodontal therapy is to reduce the PD and gain clinical attachment which would allow for the patient to better clean their mouth; better access for professional care which would allow for a healthy oral environment. It is not different for corrective surgical treatment. Except now in order to properly clean the area the surgeon must have access to the area by reflecting a soft tissue flap. Corrective surgical

therapy may be OFD; osseous resective therapy, or regeneration. All of these forms of treatment require a flap to be reflected so that the bone and roots can be accessed. OFD implies that a flap is reflected; the defect is debrided and the roots are cleaned via SRP. The flap is then sutured back in place and allowed to heal. This may be a good surgical option for shallow defects however this would not be a good treatment decision for moderate to deep defects. Osseous resective surgery is basically the same as OFD however some of the soft tissue is remove or is apically positioned and the non-supporting alveolar bone is plastied and ostectomy of supporting bone to allow for a positive bony architecture (Selipsky, 1976; Tibbetts L, Ochsenbein C, Loughlin D, 1976; Ochsenbein, 1986). The site is then sutured and allowed to heal with more tooth structure exposed to the oral cavity. The down side to osseous resective surgery is the possibility of sensitivity due to root exposure and esthetic concerns due both root exposure and long appearing teeth. In contrast, with periodontal regeneration the soft tissue is not usually resected however the bone may be slightly recontoured to better develop the site for graft containment. Like OFD and osseous resective therapies the defect is debrided and the roots are cleaned. The defect may now receive monotherapy: cover the defect with a membrane, GTR; bone graft placed into the defect without a membrane; or combination therapy, placement of a bone graft followed by coverage with a membrane. The site is then sutured gaining primary closure (proximation of the wound edges). Although all three forms of regeneration is effective it has been shown that combination therapy is the most effective in the long term (McClain, 1993; Luepke, 1997; Reynolds, 2003; Avila-Ortiz, 2015).

Guided Tissue Regeneration

Nyman is credited with completing the first guided tissue regeneration (GTR) procedure in 1982. Since Nyman's initial use of GTR, many dentists as well as Nyman have tried to improve techniques and materials to make completion of GTR more user friendly. However when completing GTR procedures one must consider several factors. Factors that influence how much regeneration occurs were documented in 1986 by Gottlow et al. Gottlow stated that "the degree of gingival recession that occurs during healing; the morphology of the periodontal defect, and the amount of remaining periodontum are all factors to consider when planning GTR. GTR is a procedure in which three of the four tissues of a diseased periodontum are regenerated and the fourth is excluded by a member barrier. The bone, cememtum and periodontal ligament are desired tissues for regeneration as they contain cells which form those structures. The periodontal ligament contains cells which can produce all three components (Gottlow 1982). When grafting one must always consider the three factors stated earlier by Gattlow however, morphology and remaining periodontum seem to be a bit more important.

When considering morphology the number of walls a defect has is important. It is known that a three walled defect is the most predictable followed by a two wall defect. One and zero wall defects are difficult to obtain good bone fill. The remaining periodontum goes somewhat hand in hand with morphology however it takes into account the width and depth of the defect. Deep, narrow followed by shallow, wide defects are better for grafting as blood supply would be greatest and one would likely

get regeneration up to the alveolar crest. On the other hand deep, wide defects would have less blood supply coming from the surrounding bone and thus not the best defect for grafting procedures. Overall deep, narrow, three wall defects are the most predictable and favorable sites for GTR (Becker W, Becker B; 1993). According to one study the average bone fill of intrabony defects using GTR are: three wall 95%, two wall 82% and one wall 39% (Cortellni 1993). That study also found that there was a 4.7mm reduction of the intrabony defect and that 90% of the sites gained 2mm or more of bone fill and no site lost supporting bone. The fourth tissue of the periodontum is the epithelium which is excluded in GTR. If the epithelium is not excluded then one is likely to get more epithelium than the other three structures which are important in securing the tooth. The more bone, cementum, and periodontal ligament that can be regenerated around the tooth the better or more successful the GTR procedure especially if one can achieve a long term outcome and there have been reports greater than fifteen years (Cortellini 2004).

GTR can be done without or with a bone graft (combination therapy) and with apparently the same success rate as with bone grafts (Trejo 2000). Trejo found that when comparing GTR to GTR with a bone graft that PD, CAL and recession were not statistically different. However Luepke (1997) found in a study comparing the use of a bioresorbable membrane with and without DFDBA and found that the use of a bone graft increased vertical bone height in furcations. In a different study comparing GTR to combination therapy; it was found that sites treated with a bone graft were more stable over the 5 year period. The results of that study also showed that more furcation sites

obtained complete bone fill and maintain the bone fill when compared to the site treated by GTR alone. (McClain, 1993)

Although GTR is an effective form of treatment for bony defects the long term stability of sites treated with combination therapy has better success. The ultimate fate of a bone graft is to turnover into the patient's bone and that turned over bone should be unified with the surrounding bone. Although an autograft has bone forming cells within the graft the patient may not want to have a second surgical site to obtain bone. An allograft maybe a good alternative as a second surgical site is not required. The autograft may have the osseogenic advantage over allografts specifically DFDBA in and extraction socket (Becker, 1994) however it has been shown that allografts are effective in GTR procedures. Mellonig (1984) found in a study with 32 test teeth and 15 controls, open flap debridement, having a reentry period of 6-13 months that there was greater bone repair 2.57mm and less crestal bone resorption 0.47mm than in sites not treated with a bone graft which had 1.26mm of repair and 1.26mm of crestal bone resorption. They also had a CAL gain of 2.91mm with the bone graft compared to 1.53mm in the sites not receiving a bone graft. That study also presented the data in percentage of bone fill. The sites treated with DFDBA had 78% of sites with complete or greater than 50% bone fill whereas the control had only 40% have complete or greater than 50% bone fill.

Materials Used in Combination Therapy

Root Surface Conditioners

Several types of root surface cleaners or conditioners have been used to assist cleaning the tooth's root surface in periodontal regeneration. Citric acid, tetracycline

and ethylenediaminetetraacetic acid (EDTA) are a few examples of root surfaces conditioners that have been used. According to a systematic review the use of these products to modify the root surface had no benefit with regards to improvement in the clinical outcome over scaling and root planning alone (Mariotti, 2003). However in an in-vitro study testing tetracycline HCL showed that tetracycline treated root surfaces increased the binding of fibronectin which in turn stimulated fibroblast attachment and growth as well as subduing epithelial attachment and growth. (Terranova et al, 1986). This study demonstrated that tetracycline HCL had a positive effect on fibroblast growth and a negative effect on the growth of epithelium. In a comparative study viewing extracted teeth under SEM showed that teeth treated with tetracycline HCL or citric acid (pH=1) for 5 minutes without burnishing showed removal of the smear layer thereby exposing the dentinal tubules and rendering a surface devoid of debris found on surfaces that had only been root planned (Lafferty, 1993). Therefore both tetracycline and citric acid had the ability to better cleanse the root surface better than root surfaces that were only scaled and root planned. 24% EDTA can provide the same results as citric acid and tetracycline according to a study completed on teeth that were SRP only, SRP and treated with EDTA or treated with EDTA only then immediately extracted and viewed under scanning electron microscope (SEM) or used to culture human PDL fibroblast for 24 hours. In that study it was found that the SRP only teeth as well and the EDTA treated only teeth still had areas of bacterial accumulation and a failure of PDL cells to adhere to the root surface. However teeth that had been SRP followed by 4 minutes of EDTA treatment the smear layer was removed and round to oval dentinal tubules were exposed along with the observations of collagen fibrils. This group also

showed a significant increase in the number of fibroblast cell attachment (Gamal, 2003). This proved that EDTA could remove the smear layer providing a cleaner surface with a greater potential for cells to attach and grow.

Bone Grafts

In combination therapy, a bone graft is utilized and can be autografts, allografts, isografts, xenografts, or alloplast. These bone grafts may have osteogenic, osteoinductive or osteoconductive capabilities. The purpose for using the specific type of bone lies within the properties of the graft used; however, the end result of its use is always to see a clinical and or radiographic increase in bone. It has been shown in many studies that a membrane without bone grafting can increase the fill of bone in defects (Bowers 1989, Becker 1993, Cortellini 2004). However there have also been studies which found that the addition of a bone graft (DFDBA) with a membrane had no extra benefit when compared to a membrane alone (Chen 1995, Gottlow 1986). Altiere in 1979 reported that "nongrafting procedures may be more effective in generating new attachments or reattachments in human periodontal osseous defect than previously believed." All be it, a 2003 systematic review by Reynolds showed that combination therapy in general had a greater benefit due to their ability to decrease crestal bone loss and increase bone levels.

Autografts are transferred from one site to another site in the same individual (American Academy of Periodontology Glossary of Periodontal Terms 2001) and has the greatest potential for osteogenesis because it contains osteoblast from the patient.

Autografts can be taken from the maxillary tuberosity, the ramus, tori, exostoses or from a recent extraction site to name a few.

Allografts are transferred from genetically dissimilar individuals of the same species (American Academy of Periodontology Glossary of Periodontal Terms 2001). They can be osteoconductive or osteoinductive. Allografts are divided into two categories freeze dried bone allograft (FDBA) and demineralized freeze dried bone allograft (DFDBA). FDBA is only osteoconductive meaning it can only be used as a scaffold for bone to form on. DFDBA is potentially osteoinductive because it contains exposed growth factors, collagen, and BMP which can induce the surrounding tissues to produce osteoblast which produces bone. Urist, in 1975, discovered that human bone could undergo chemical extraction that would make it useful as a bone graft material. A study completed by Bowers (1989) found that intrabony defects grafted with DFDBA had an increased amount of collagen, bone and periodontal ligament and therefore enhanced new attachments apparatus formation and labeled DFDBA as osteoinductive. However, Becker in 1994 reported that the study he conducted "questions the use of DFDBA as a bone inductive graft material." Although some authors may question the use of DFDBA in GTR procedures, DFDBA has been used successfully for GTR procedures in humans for almost 30 years. (Bowers, 1989).

Now a product distributed by Keystone Dental, Accell Connexus®, is a new bone allograft material approved by the FDA for periodontal regeneration. It is contains DFBBA within a proprietary poloxamer reverse phase medium. The medium permits the material to have a putty consistency and allows the practitioner to mold and shape

the bone graft. Because it is moldable it is believed that Accell Connexus® will maintain its shape and remain in place better than particulate DFDBA. Accell Connexus® undergoes a slightly different processing from traditional DFDBA. The additional step involves splitting a large sample of DFDBA into two parts. One part is dissolved releasing growth factors and bone proteins that are isolated and extracted. That extract is then added to the other half of the DFDBA and the reverse phase medium. This process results in the increased concentration of BMP compared to traditional DFDBA allowing Accell Connexus® to have 5-7 times more BMP than the particulate DFDBA (Company information, Keystone Dental). The bone graft is then sterilized in the same manner as particulate DFDBA which has been shown to preserve growth factors.

Isografts are from genetically identical individuals, usually identical twins (American Academy of Periodontology Glossary of Periodontal Terms 2001). They are much like allografts however these grafts contain the same genetic make-up of the individual receiving the graft.

Xenografts or heterografts are from a different species (American Academy of Periodontology Glossary of Periodontal Terms 2001). These grafts are usually bovine, equine or porcine when it comes to use in humans. They are only osteoconductive .

Alloplast are synthetic or inert foreign body implanted into tissue (American Academy of Periodontology Glossary of Periodontal Terms 2001). They are materials such as bioactive glass, calcium sulfate or beta tri- calcium phosphate and are only osteoconductive.

Barrier Membranes

Biologic membranes have been used to assist in the regeneration of bone, cementum and the periodontal ligament. It is believed that if the gingiva, primarily the epithelium, is excluded regeneration of the underlying periodontium can take place. However if no barrier is present to prevent the epithelium from growing into the site of regeneration then the new attachment will more than likely be long junctional epithelial (Bunyaratavej 2001). The junctional epithelium will reattach to enamel, cementum, dentin and in some conditions calculus (Melcher 1976). Because epithelium grows at a rate of 0.5mm per day which is faster than bone, cementum and the periodontal ligament (Engler 1966) inhibiting these non-osteogenic cells from infiltrating the regeneration site seems ideal. For that reason barrier membranes were introduced into dentistry in the early 1980's. The first membranes were nonresorbable and required a second surgery for removal. Not only do non-resorbable membranes require a second surgery to be removed there were also problems associated with early membrane exposure (Schallhorn, 1994). The resorbed membranes were introduced in dentistry the late 1980's and eliminated the need for a second surgery because these membranes resorbed. However with the ability to resorb these membranes were subject to a faster resorption when exposed to the oral environment. Therefore gaining primary closure is very important to prevent a more rapid breakdown of the barrier membrane.

Nonresorbable verse Resorbable Membranes

Both nonresorbable and resorbable membranes can be used in GTR. Some authors have reported that with nonresorbable membranes there is an increase in soft

tissue complications due to the membrane becoming exposed. Tal 2008 completed a study on crossed linked and non-cross linked collagen membranes and found that 50% of cross linked collagen membranes became exposed compared to 23.1% of non-cross linked membranes. Although collagen membranes can also become exposed it seems that resorbable membranes have become more popular. Zitzmann et al. 1997 stated that with Gor-Tex, a nonresorbable membrane, had "44% wound dehiscences and/ or premature membrane removal occurred" and that Bio-Gide, a resorbable membrane, was "a useful alternative." In a clinical comparative study between bioresorabable and non-resorbable membranes Cortellini and colleagues (1996) concluded that clinically significant CAL gains can be obtained with GTR procedures with both types of membranes however less issues were associated with the bioresorbable membranes.

Nonresorbable Membranes

Polytetrafluroethylene (ePTFE) is comprised of a carbon chain with two fluorine atoms for every carbon atom. The complete fluorination of the carbon chain, along with the strength of the carbon-to-fluorine bonds, makes PTFE highly stable. This stability results in a synthetic polymer that is non-resorbable, biologically inert, chemically non-reactive (www.osteogenics.com cited 2012 October 30) and must be removed. Examples of PTFE are Gor-Tex which was the first non-resorbable membrane on the U.S. in the 1980's and Cytoplast placed on the U.S. market in 1997 (www.osteogenics.com cited 2012 October 30).

Synthetic Resorbable Membranes

These membranes are made from synthetic materials such as glycolide and trimethylene carbonate copolymer fiber or glycolide and lactide copolymer (www.goremedical.com cited 2012 October 30). Examples are Vicryl Mesh Polyglactin 910 and Polyglycolin Acid (Resolut XT).

Natural Resorbable Membranes

Collagen membranes are type I and/ or type III collagen from cows or pigs and can be either cross-linked or noncross-linked. These membranes are hydrolyzed or enzymatically degraded (Duskova et al.) therefore do not require removal. According to one author "collagen membranes have the following properties: hemostasis, stimulation of fibroblast by chemotaxis, acts as a support construction for the migration of fibroblast to periodontal ligaments, easy to shape and adapts well to root surfaces, has low antigeneicity and immunogenicity, and eliminates the need for a second surgery because they are bioabsorbable" (Duskova M, et al, 2006). A few examples are Bio-Gide porcine membranes, Biomend and Biomend Extend bovine membranes.

Table of Types of Collagen Membranes

Name	Company	Source*	Cross Linked (C) / Noncross Linked (N)*	Resorption Rate*
Bio-Gide	Geistlich	Porcine dermis collagen type 1 and 3	N	24 weeks
Biomend	Zimmer	Bovine collagen type I	Formaldehyde	8 weeks
BioMend Extend	Zimmer	Bovine collagen type I	Formaldehyde	18 weeks

Table 1: Examples of collagen resorbable membranes.
*Company Information

Membranes are derived from human tissues have been shown to have grater biocompatibility and immunogenicity (Xenoudi 2011, Chen 2010, Park 2009, Niknejad 2008, Duskova 2006, Kubo 2001). It has also been reported that they allow for more rapid healing. One study reported, three days after surgery, the site containing a cryopreserved amniotic membrane had more epithelialization than the control site which did not contain a membrane (Valaz 2010). However that study also reported that at two weeks both the sites containing the membrane and the control were clinically equal. Dura Mater, Pericardium, and Placenta are donated human tissues that have been utilized as membrane barriers.

It seems that the use of a resorbable or nonresorbable membrane in GTR procedures is acceptable. However the clinician must use their clinical judgement as to which membrane is best for the patient.

Soft Tissue (Gingiva) Closure

The soft tissue covering the membrane should have primary closure and heal rapidly. Rapid healing of the soft tissue from all sides is usually desired whenever a wound occurs and there is scientific evidence that the healing of wounds occurs from all borders regardless of the type of tissue being repaired (Cutright 1969). Epithelium is one of the fastest growing tissues as reports by Engler 1966. Engler found that epithelium grows at a rate of 0.5mm per day. Although in many situations it would be highly desired to have a wound heal with epithelium, it is not the tissue surgeons consider ideal when it comes to GTR. One would rather have cells which form connective tissue, cementum and bone. Over the years many techniques have been tried to eliminate epithelial cells from infiltrating grafted sites. One method left denuded bone at the time of mucoperiosteal surgery leaving the epithelium with a longer distance to travel than the connective tissue. Because of this one would get a connective attachment ahead of a long epithelial attachment (Pfeifer 1963). As one could imagine, this procedure was reported in Pfeifer's article as painful. Therefore it is better to have bone covered during the healing process to prevent pain and possible infection.

The keratinized stratified squamous epithelium of the oral epithelium is in place to withstand the forces of brushing, flossing, food particles contacting the gingival and

etcetera. Sulcular epithelium is an extension of the oral epithelium however lacks keratinizaton. Sulcular epithelium is on average 0.69mm (Gargiulo 1961). The extension of the sulcular epithelium is the junctional epithelium and on average in a normal healthy periodontium as reported by Gargiulo 1961 is 0.97mm. The junctional epithelium often interferes with the desired healing in GTR if no barrier is in place to exclude it. In the event that the junctional epithelium grows past its normal resting place during wound healing it would then be called the long junctional epithelium. Apical to the junctional epithelium is the connective tissue attachment which contains collagen type I, III and IV. The connective tissue contains gingival fibers which hold the free gingiva up around the tooth like rubber bands which runs in different directions. The connective tissue also anchors the gingival corium to the bone via Sharpey's fibers and is the final protective barrier prior to the bone. The gingival tissue is tightly bound to the bone by its basement membrane. In an animal study completed by Hiatt et al. in 1968 found that it took 225 grams of force on silk sutures to separate a flap from the tooth and bone after two to three days of healing following mucoperiosteal flap surgery and at two weeks the tissues could be partially separated using 340 grams. However using 1,700 grams of force after four to six months of healing the sutures pulled through the tissues leaving the flap intact. This also demonstrated that "the strength of the epithelial attachment to the root is greater than the attachment between cells (Hiatt 1968). Although one would prefer a connective tissue attachment during would healing it has been demonstrated in an animal models that a long junctional epithelium may be just as effective as the connective tissue attachment to inflammation (Beaumount, 1984) and the length of the long junctional epithelium does not play a role of gingival health

(Magnusson, 1983). Although a connective tissue attachment may show no advantage over a long junctional epithelium attachment in the animal model regeneration implies that one would prefer the connective tissue attachment.

This review of the literature addressed periodontitis and periodontal regeneration as it relates to intrabony defects utilizing the GTR techniques. Because there are no published studies comparing DFDBA and Accell Connexus®, the present study will address GTR as it relates to the comparison between DFDBA and Accell. This study will attempt to find a difference in PD reduction; CAL gain, recession, as well as gain in radiographic bone fill with the use of a Bio-Gide barrier membrane. Therefore the objective of this research is to determine if Accell provides superior regeneration compared to traditional DFDBA in intrabony defects. The hypothesis is that Accell Connexus® provides periodontal regeneration that is superior to traditional DFDBA. The sites treated with Accell will have better outcomes with respect to greater clinical attachment level gain, which is the primary outcome measure, greater decrease in probing depths, and more radiographic bone fill.

CHAPTER III
MATERIALS AND METHODS

Thirty subjects diagnosed with severe periodontitis are being enrolled in the study. (Please see Appendix A1 for a flow diagram of the proposed study.) The findings of their comprehensive periodontal evaluation such as probing depths (PD), clinical attachment levels (CAL), and recession were recorded on the Navy Periodontal Chart Form - NAVMED 6660/2 (appendix B2) by the subject's provider. Patient who met the inclusion criteria (Please see Appendix ***for inclusion/ exclusion check list.) for the study, were offered the opportunity to participate. The methodology for this study is listed below in sequential order.

The inclusion and exclusion criteria for this study included the following:

Inclusion Criteria

a. Patient aged ≥18 years old
b. Patient will be remaining in the Capital region for at least 12 months following the surgical procedure for follow up appointments
c. Diagnosis of generalized or localized severe periodontitis
d. Radiographic evidence of a vertical intrabony defect at one or more sites with a probing depth ≥ 6 mm
    i. If the patient present with more than one defect site meeting inclusion criteria, the site with the deepest probing depth will be used in the study

Exclusion Criteria

a. Patient under the age of 18
b. Patient will be moving from the Capital region area prior to 12 months following the surgical treatment
c. Furcation involvement in combination with the intrabony defect determined pre-surgically

d. Patients with restorations extending beyond the cementoenamel junction at the intrabony defect site
e. Patients with an indiscernible cementoenamel junction either clinically or radiographically
f. Patients with periapical pathology, unrestored caries, defective restorations, root resorption, or vertical root fracture
g. Patients requiring restorative dental care (fillings and crown and bridge work) that cannot be completed prior to fabrication of the customized stent
h. Female patients who are pregnant or nursing
i. Patients who currently smoke tobacco or use tobacco products. Former smokers will be excluded if they quit smoking < 6 months prior to selection in the study.
j. Patients with clinically significant systemic diseases, which may affect healing (e.g. uncontrolled diabetes).
k. Patients allergic to chlorhexidine gluconate (Peridex).
l. Patients allergic to tetracycline
m. Patients with poor oral hygiene unsuitable for periodontal surgery
n. Patients who cannot or will not sign the informed consent form
o. Patients receiving immunosuppressive therapy such as chemotherapy and systemic corticosteroids not to include inhaled or topical steroids
p. Patients with severe endocrine-induced bone diseases (e.g. hyper-thyroidism, altered parathyroid function)
q. Teeth with intrabony defect have mobility classified as Miller class 2 or greater
r. Patients with bleeding complications (e.g. hemophilia)
s. Patients on warfarin therapy
t. Patient with a history of osteoporosis or taking bisphosphonate medications
u. Patients with a history of radiation therapy in the head and neck area

Initial Sequence:

1. Patient is referred for a comprehensive periodontal evaluation.
2. Initial therapy in the form of scaling and root planing is accomplished by a registered hygienist, periodontist, or periodontal resident.
3. 4 to 6 weeks following initial periodontal therapy, the patient's initial therapy is re-evaluated to assess healing and oral hygiene.
4. A 2nd full periodontal charting will be completed at re-evaluation; including probing depth measurements, clinical attachment level measurements, bleeding on probing, and plaque scores for each tooth.
5. Based on the re-evaluation a treatment plan will be developed for each patient. Typical treatment plans are:
    a. Maintenance therapy. No surgical treatment required; patient is not a candidate for the study.
    b. Surgical treatment required, but regenerative therapy is not indicated, the patient is not a candidate for the study.
    c. Intrabony vertical defect is present, but site has furcation involvement. The patient is not a candidate for the study.
    d. Intrabony vertical defect is present and regenerative therapy is the treatment of choice.
        - Patient will be asked if he/she would like to participate in the study and will then be provided a one page brief about the study
            i. If the patient consents to be in the study, the therapy will continue as stated below
            ii. If the patient does not consent to be in the study, surgical therapy will continue as planned by the patient's surgeon.

Following Consent:

1. Maxillary and mandibular impressions using an irreversible hydrocolloid material (alginate) will be made using stock impression trays; sized small, medium, or large depending on the size of the subject's mouth. The impressions will be poured with dental stone. The stone models of the subject's jaws will be used to fabricate a customized plastic stent to allow standardized measurements of the surgical site.
    a. Plastic stent fabrication:
        i. A plastic stent for making probing depth measurements will be fabricated utilizing the methods described by Isador 84 and Deas 04.
        ii. A 2 mm thick co-polyester plastic dental splint material (biocryl material) will be adapted to the stone model of the subject's arch utilizing a BioStar matrix machine.
        iii. The stent will be trimmed to end just above the height of contour of the crowns of the teeth in order to visualize the gingiva.
        iv. A fissure bur (1169 bur) will be used to cut grooves in the interproximal areas and along the buccal and lingual aspects of the teeth being investigated. These grooves accommodate the periodontal probe and allow the investigator to probe the same location and with the same angulation at pre or post-surgical visits.
        v. Following use the stent will be cleaned and disinfected with Dispatch spray and stored in a ziplock plastic bag labeled with the subject's study number. The bag will be locked in a secured drawer maintained by the primary examiner; and then retrieved for measurements at 6 and 12 months.

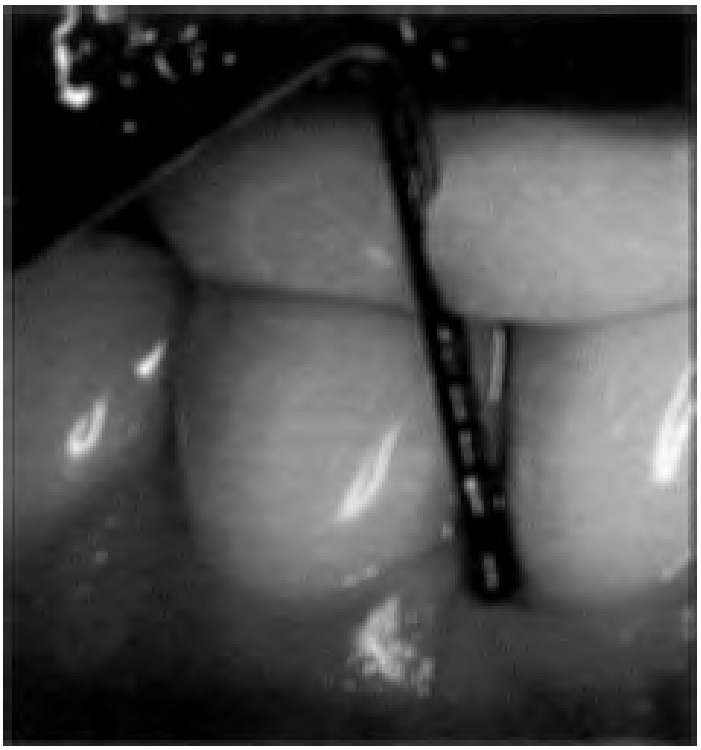


Fig 6: Example of the customized stent used for data collection Used with permission from the author of this thesis, LCDR Teresita Alston.

2. A customized bite-plate registration using the paralleling radiographic technique will be fabricated for each patient to standardize radiographs at baseline and 6 and 12 months after surgery.
    i. A Rinn film holder used for the paralleling technique will be selected based upon the size of the sensor used for the digital radiographs:
        1. Size 1 for individuals with smaller mouths
        2. Size 2 for individuals with larger mouths.
    ii. Blu-mousse, a bite registration material, will be applied to each side of the film holder where the teeth contact the holder>
        1. Subjects bite into blu-mousse until the material hardens (approximately 45 seconds).
        2. The film holder is removed from the mouth.
        3. The film holder is reinserted into the mouth and the subject bites down to confirm that the bite is reproducible.

iii. *Following use, the film holder will be cleaned and disinfected with Dispatch spray and stored in a ziplock plastic bag labeled with the subject's study number and locked in a secured drawer maintained by the primary examiner; and then retrieved for postoperative radiographs at 6 and 12 months.

Fig 7. Sample customized holder for standardized radiographic using Blu Mousse bite registration material Used with permission from the author of this thesis, LCDR Teresita Alston.

3. Prior to surgery, clinical parameters will be measured using the customized plastic stent* and a UNC-15 periodontal probe. All clinical measurements will be made by a blinded study investigator.
    a. Probing depth: measured in millimeters from the gingival margin to the base of the pocket.
    b. Clinical attachment level: Measured from the cementoenamel junction of each tooth to the soft tissue base of the pocket.
    c. Recession: Measured from the cementoenamel junction of the tooth to the gingival margin.
    d. Bleeding on probing: 30 seconds following measurements of the probing depth and clinical attachment level, the area will be re-examined.
        i. The presence or absence of bleeding will be recorded on the data collection sheet.
    e. Plaque score: The presence or absence of plaque at the defect site will be recorded on the data collection sheet.
4. Prior to surgery, a standardized digital periapical radiograph will be made using the customized bite-plate and the paralleling technique.
    a. All radiographs made at NPDS are stored on the NNMC-DDILOCAL radiographic database and are viewed using the software XrayVision DCV. This database is secured. The database can only be accessed by authorized CAC users. Radiographs are identified by the patient's full name, social security number and date image was made.

Randomization Procedure:

1. A computer program will randomly sequence each subject's study enrollment numbers (1-30) as in the example below.
    a. A random sequence table will be generated by the research coordinator following IRB approval in order to maintain blinding of investigators.

Table 2. Sample Random Sequence Generator:

http://www.random.org/sequences/?min=1&max=30&col=2&format=html&rnd=new

Group A. DFDBA	Group B. Accell
2	4
25	15
30	28
14	10
24	6
1	21
11	7
5	26
19	17
13	9
16	12
22	23
3	20
29	27
18	8

Timestamp: 2012-05-31 18:54:03 UTC

2. Thirty envelopes marked 1 -30 will contain either a card stating DFDBA or Accell. Thereafter, the random sequence table will be placed in a sealed envelope that will not be opened until all data has been collected. Sealed envelopes (1-30) will be stored by the principal investigator in a locked drawer.
3. When each participant goes to surgery the investigator will provide the surgical team the envelope corresponding to that subject's enrollment number. The surgical team will open the envelope and remove a card which will state which bone graft material to place following debridement and categorization of the defect.
    a. A surgical team member will check on the card whether the intrabony defect was ideal for bone grafting, $\geq$ 4mm in depth or less than ideal, < 4mm in depth, and if a furcation was evident that was not detected pre-surgically.
        i. Please note that surgical findings sometimes differ from pre-surgical estimates of the surgical site.

        One of the cards below will be sealed in each envelope (1-30).

Accell	
__ defect≥4mm	__ defect<4mm
	__ furcation evident

DFDBA	
__ defect≥4mm	__ defect<4mm
	__ furcation evident

4. The completed card will be returned to the numbered envelope and resealed. The study investigator will collect the sealed envelope and place it in the data collection folder for each study participant that is stored by the principal investigator in a locked drawer.
5. The study investigators who make the postsurgical clinical and radiographic assessments at 6 and 12 months will be blinded to which bone graft material a given participant received.

Surgical Procedure:

Females of child bearing age will be asked to complete a HCG (human chorionic gonadotropin) urinalysis prior to the surgical procedure. If the results of the HCG test are positive, the subject will be exited from the study.

Prior to surgical procedure, in line with standard procedure at the Periodontics Department participants will be offered the option of having the surgery performed using: 1. only local anesthesia, or 2. a combination of oral anxiolysis with Triazolam and local anesthesia, or 3. a combination of IV moderate sedation with Versed and Fentanyl and local anesthesia. The use of sedation will not affect the surgical procedure.

1. The surgical provider will be either a board certified staff periodontist or a 2nd or 3rd year periodontal resident. All surgical providers will be briefed in the protocol. All surgeries will follow the same steps listed below.
    a. Surgical set-up is standardized for all surgeries done at the Naval Postgraduate Dental School Periodontics Department.
    b. Both the experimental (Accell) and control (DFDBA) materials will be available to the surgeon. The bone graft material used will be determined when the sealed envelope is opened by a surgical team member after the defect has been debrided and characterized.
    c. Surgical Procedure Steps:
        i. Placement of normal saline IV
            1. Administration of 8mg Dexamethasone IV
        ii. Administration of oral anxiolysis or IV moderate sedation if patient desired and indicated
        iii. Administration of topical and local anesthetic with any combination of 2% Lidocaine with 1:100K epinephrine, 4% Articane with 1:100K epinephrine, and 0.5% Marcaine with 1:200K epinephrine
        iv. Sulcular incisions and full thickness reflection of the surgical flap
        v. Debridement of the surgical site/defect to remove granulation tissue and calculus using hand instruments and cavitron ultrasonic instrument
        vi. Characterization of the defect by a study investigator

1. Number of defect walls present: 1-, 2-, 3-walled defect or combination defect
2. Depth of defect from CEJ to the base of the bony pocket
3. Depth of defect from the alveolar crest to the base of the bony pocket
4. Mesial-distal defect width: Measured in the mesial-distal direction from the tooth to the mesial or distal margin of the defect
5. Buccal-lingual defect depth: Measured in the buccal-lingual direction from the buccal margin of the defect to the lingual margin of the defect
6. Following defect characterization, the investigator provides the surgical team with the sealed envelope to determine which bone graft material, Accell or DFDBA, the participant was randomized to receive, and the investigator leaves the surgical suite.

vii. The graft material will be prepared as defined by the manufacturing instructions:
   1. Hydration of the graft material with sterile saline - DFDBA
   2. Graft material dispensed from syringe - Accell.

viii. The root surface of the tooth bordering the defect site will be treated with a 24% EDTA gel f for 4 minutes. The site will then be washed with sterile saline for 1 minute.

ix. Osteoplasty (reshaping unsupported the alveolar bone) will be performed as needed

x. Intramarrow penetration of the bone within the defect using a ¼ surgical round bur to induce bleeding in the defect site

xi. Graft material (determined from the sealed envelope) placed into the defect up to the level of the alveolar crest

xii. Bio-Gide membrane trimmed and positioned to cover grafted defect

xiii. Primary flap closure achieved using a non-resorbable monofilament suture (ie. Gore-tex)

xiv. Gauze pressure will be held on the site for 5 minutes to achieve

hemostasis and reduce the size of the fibrin clot formed.

xv. Periodontal dressing may be placed over the surgical site.

xvi. Surgical team checks appropriate findings on randomization card, reseals card in envelope, and envelope collected by investigator.

1. Envelopes will not be re-opened until after data analysis

Figure 8. Hydrated DFDBA

Figure 9. Accell Connexus®

Post-operative Care:

1. All participants receive the following post-operative regimen:
    a. Pain medication consisting of any of the following alone or in combination:
        i. Ibuprofen 800 mg , Take 1 tab PO q6-8h for moderate pain
        ii. Hydrocodone/Acetaminophen 5/325 mg, Take 1-2 tab PO q6h prn severe/breakthrough pain
        iii. Oxycodone/Acetaminophen 5/325mg, Take 1-2 tab PO q6h prn severe/breakthrough pain

b. Pain medication for patients who cannot take NSAIDS will be prescribed any of the following alone or in combinations:
    i. Acetaminophen 325 mg, Take 1-2 tabs PO q4h for moderate pain
    ii. Oxycodone 5mg, Take 1 tab PO q4h prn severe/breakthrough pain
c. Antibiotics consisting of either of the following:
    i. Amoxicilin 500mg, Take 1 tab PO q8h for 10 days
    ii. Clindamycin 300 mg, Take 1 tab PO q8h for 10 days
d. 0. 12% Chlorhexidine, 1 bottle, Rinse and spit bid with 1 TBSP as directed on the bottle

2. All patients are provided with the standard post-operative instructions (See appendix B3 for an example of the standard postoperative care instruction form).
3. Patients are recalled at 1 week to assess post-operative healing and remove plaque/deposits on the surgical site.
4. Patients recalled at 2 weeks post-operative to assess healing, remove plaque, and remove sutures at the surgical site.
5. Patients recalled at weeks 4, 6, 8, 12, and 16 to assess healing, remove plaque, and reinforce oral hygiene.
6. Patients recalled at 6 months following the surgical procedure to assess healing, remove plaque, and reinforce oral hygiene.
    a. A study investigator blinded to the graft material used will evaluate the periodontal parameters using the customized stent and take a periapical radiograph using the customized bite-plate and paralleling technique.
        i. Same methods as in pre-surgical evaluation
        ii. If the customized stent is not stable on the patient's teeth at the follow-up appointment, the clinical data will not be used in the analysis. The radiographic data will still be collected.
7. Patients recalled at 9 months for periodontal maintenance therapy
8. Patient recalled at 12 months following the surgical procedure to assess healing, remove plaque, and reinforce oral hygiene.
    a. A study investigator blinded to the graft material used (other

than the surgeon or the staff member on the surgical case) will evaluate the periodontal parameters using the customized stent and take a periapical radiograph using the customized bite-plate and paralleling technique.

i. Same methods as in pre-surgical evaluation

ii. If the customized stent is not stable on the patient's teeth at the follow-up appointment, the clinical data will not be used in the analysis. The radiographic data will still be collected.

9. Patient will be exited from the study and followed by their primary provider for periodontal maintenance therapy.

Analysis of Data:

1. Periodontal parameters assessed at 6 months and 12 months will be compared to the baseline measurements to determine change in clinical attachment level and probing depth.
    a. A comprehensive periodontal charting (probing depths, attachment levels, bleeding on probing, plaque score) for all teeth present in the mouth will be done at the 12 months visit as well.
2. Two reviewers, board certified periodontist(s) and/or a board certified oral radiologist, blinded to which bone graft material subjects received will access the NNMC-DDILOCAL database, and use the Xray Vision software used for viewing to measure bone levels before surgery and at 6 months and 12 months.
    a. Radiographic analysis will be completed following data collection
    b. To access the radiographs, the examiners will be provided with a sub-master list containing the study number, name, and last four of the social security number.
    c. The examiners will access the patient's radiographic record on the NNMC-DDILOCAL database using the patient's name and last four.
    d. The standardized radiographs taken at baseline, 6 months following

surgery and 12 months following surgery will be obtained.

e. Using the digital radiograph software, measurements will be made and recorded on the data collection sheet for radiographs.

f. The sub-master list will be destroyed following all measurements.

3. If subtraction radiography becomes available at NPDS, the same radiographs will be used to assess changes in bone volume from baseline to 6 and 12 months postoperatively.

4. Statistical analysis will assess pre and post-test differences.

CHAPTER IV: RESULTS

A total of 21 subjects meeting the enrollment criteria between December 2012 and May 2015 were enrolled. There were 14 males and 7 females with and age range of 22-74. As of May 26, 2015 twenty subjects had surgery completed by a second or third year resident or a board certified periodontist. Of the 20 subjects 19 completed combination therapy and 1 had osseous resective therapy due to having a non-graftable defect. Three subjects were exited from the study; one due to lack oral hygiene compliance, one due to a permanent change of station, and the other due to a non-graftable defect. Probing depth (PD), relative clinical attachment level (CAL), plaque, bleeding on probing (BOP), surgical intrabony defect type and radiographic percent bone fill were assessed. Clinical and radiographic assessments were completed by two board certified periodontitis.

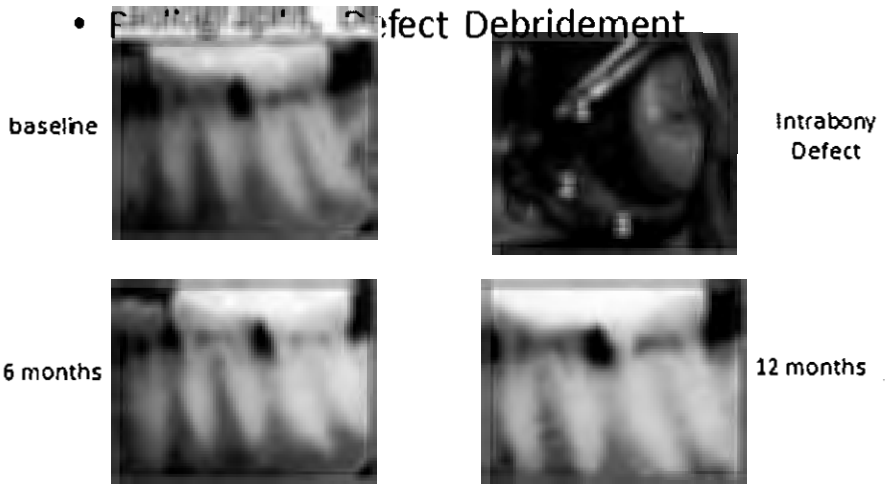


Figure 10: This is an example of a patient randomized to DFDBA. Figure 10a shows the radiographic defect at baseline. 10b shows the 3 walled defect after debridement. 10c is the 6 months post-surgical results. 10d 12 months post combination therapy. Used with permission from the author of this thesis, LCDR Teresita Alston.

Due to the enrollment status and number of exited patients 6 month and one year results were completed on 13 subjects; 7 males and 6 females with an age range of 22-67 years (mean 40.6 years). Two subjects were exited from the Accell group and 1 from the DFDBA group. Therefore 13 sets of 6month and 1 year results were analyzed with 8 subjects in the DFDBA group and 5 in the Accell group for this interim analysis.

No significant difference was found with respect to bleeding on probing (BOP) or plaque scores. The mean probing depth (PD) decreased from 7.6 (range 5.0-14.0mm) to 3.8mm (range 3.0 - 5.0mm) for Accell and from 8mm (7.0-11.0mm) to 4mm (3.0-5.0mm) for DFDBA. The mean gain of CAL was 3.4mm for Accell and 3.0mm for DFDBA. Accell and DFDBA attained positive percent radiographic bone fill; 65.79% and 59.9% respectively. The results were not statically significant.

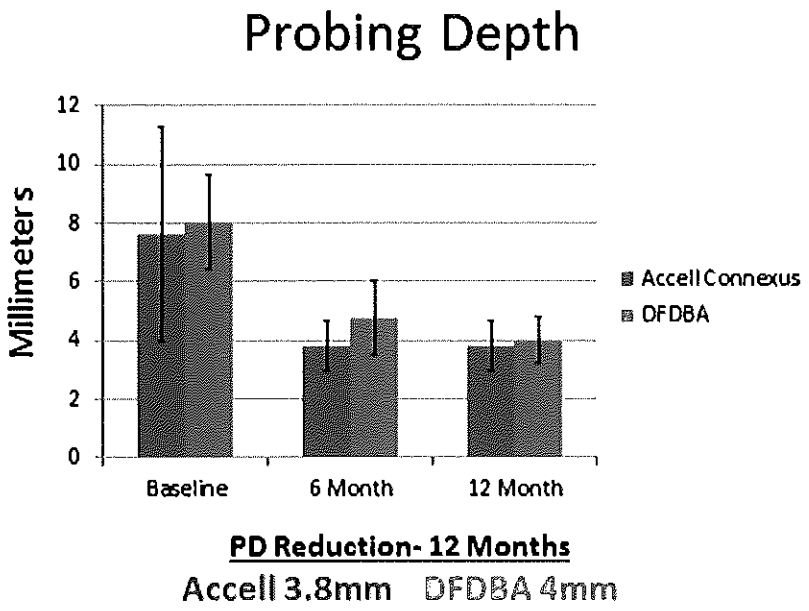


Figure 11: Probing depth at baseline, 6 and 12 months post combination therapy for Acell Connexus® and DFDBA

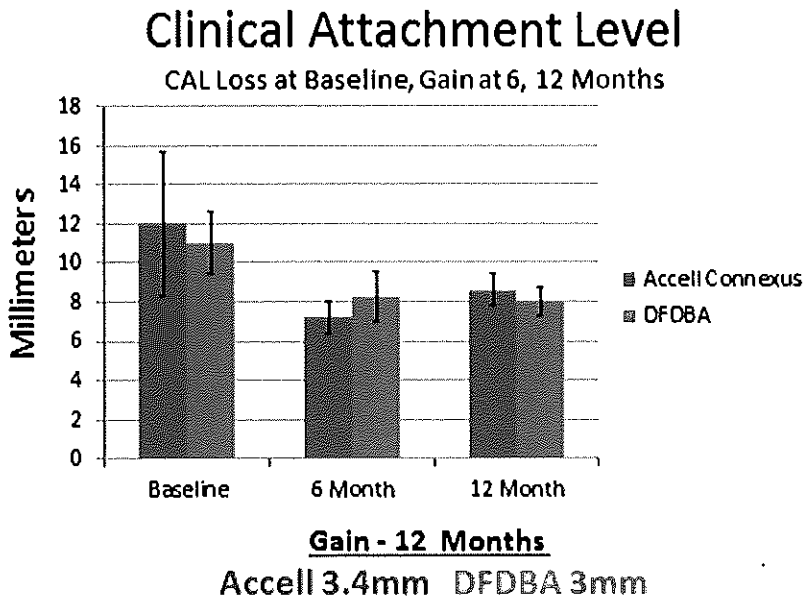
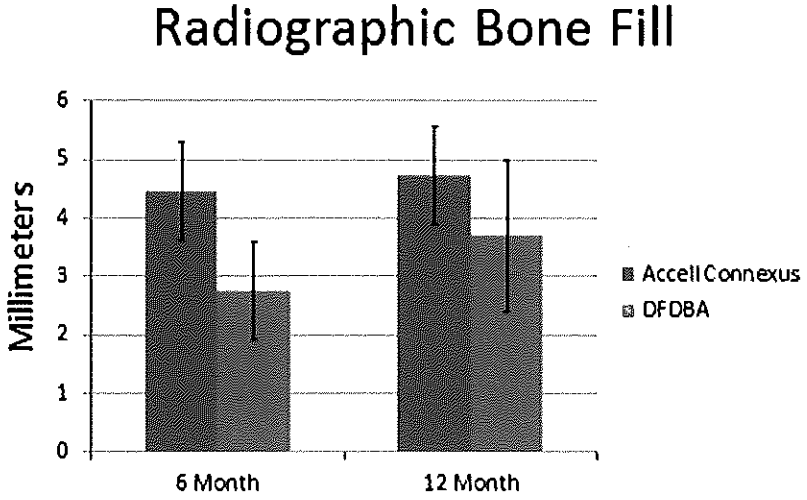


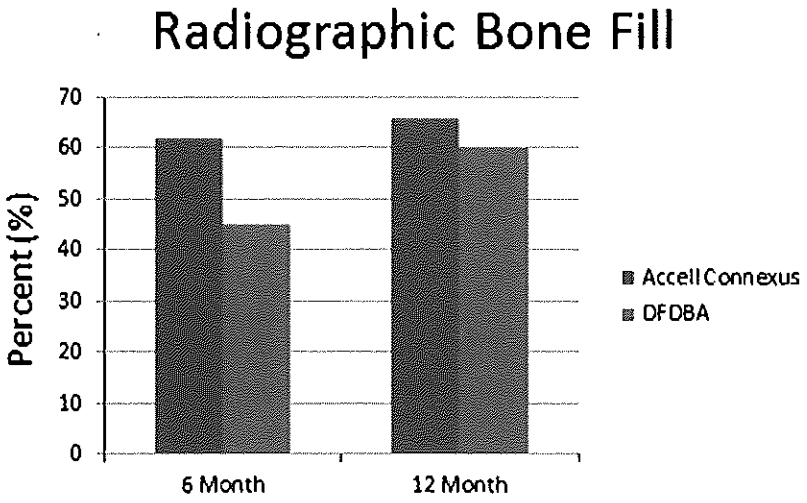
Figure 12: Clinical attachment level at baseline and 6 and 12 months post treatment.



Defect in millimeters - 12 Months

Accell 4.73mm DFDBA 3.69mm

Figure 13: Radiographic bone fill in millimeters at 6 and 12 months post treatment.



Percent Defect Fill (12 Months)

Accell 65.79% DFDBA 59.9%

Figure 14: Radiographic bone fill in percent at 6 and 12 months post treatment.

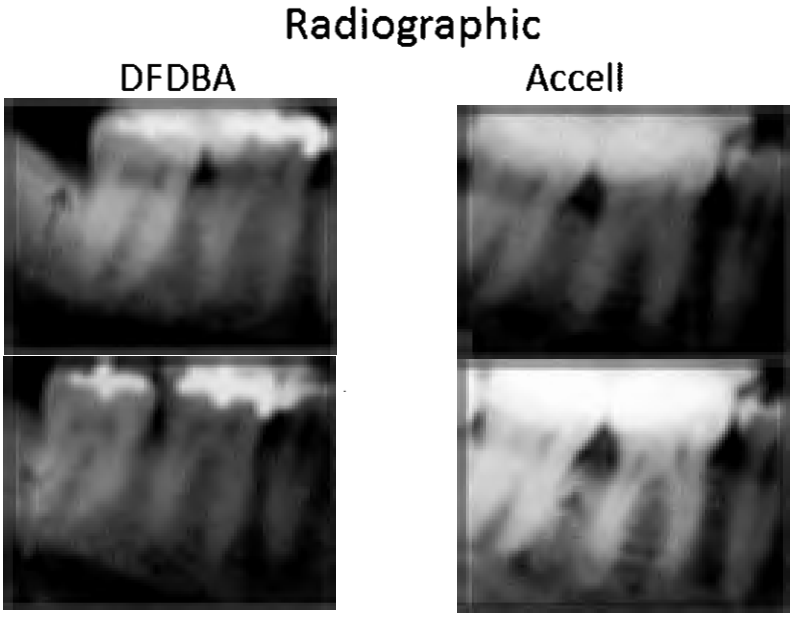


Figure 15: 15a and c are baseline radiographics of sites randomized to DFDBA and Accell respectively. 15b and 15d are the results of combination therapy at 12 months post treatment. Used with permission from the author of this thesis, LCDR Teresita Alston.

CHAPTER V: DISCUSSION

Definitive conclusions cannot be drawn at this time because 12 month clinical measurements have been made in less than half of the subjects in the approved sample size. However clinically it does appear that Accell does offer the clinical ability to allow bone apposition above the residual bony crest radiographiclly. It also appears that sites grafted with Accell are less radiopaque than sites grafted with DFDBA at the 12 months evaluation period. The makers of Accell claim that Accell is designed to release BMP immediately and over an extended period. With the extended release of those growth factors it may take longer for Accell to mature radiographiclly which may imply that 12 months is too soon to effectively evaluate the radiographic and possibly the clinical results of Accell.

The assertion is that Accell is easier to place and mold within the defect. It seems to the author that the claim is true as the material is easily placed and remained in the site. However not all providers using Accell, in this study, found Accell easy to work with. Some providers felt that the material was too soft and felt as if they could not pack the material into the defect properly.

CHAPTER VI: CONCLUSION

The data analysis at this point does not show any significant statistical difference in clinical and radiographic outcomes between DFDBA and Accell Connexus®. Both bone graft materials resulted in improved clinical parameters. Longer term follow up needs to be conducted on Accell for both clinical and radiographic results.

Appendix

Appendix A1: Raw data at baseline

Treatment Group	SubjectID	Baseline Date	Gender	Age	Tooth	Location	Baseline_ Probing Depth Buccal mm	Baseline_ Probing Depth Lingual mm	Baseline_ CAL Buccal	Baseline_ CAL Lingual	Baseline_ Recession Buccal	Baseline_ Recession Lingual	Baseline_ Plaque Buccal	Baseline_ Plaque Lingual	Baseline_ BOP Buccal	Baseline_ BOP Lingual
Accell Connexus	1	17-Jan-2013	Male	22	18	Distal	6	4	11	8	0	0	No	No	Yes	Yes
DFDBA	2	9-May-2013	Female	53	4	Distal	6	7	11	10	0	0.5	No	No	Yes	Yes
Accell Connexus	3	5-Mar-2013	Male	39	19	Distal	6	5	10	9	0	1	No	No	Yes	Yes
DFDBA	4	15-Apr-2013	Female	25	19	Mesial	6	7	11	13	0	0	No	Yes	Yes	Yes
Accell Connexus	5	15-Apr-2013	Female	45	26	Distal	7	6	11	11	0	0	Yes	Yes	Yes	Yes
DFDBA	6	24-Oct-2013	Male	47	31	Distal	7	5	11	8	0	0	Yes	No	Yes	Yes
DFDBA	7	15-May-2013	Male	32	3	Mesial	3	7	9	12	0	0	No	No	No	Yes
DFDBA	8	23-Sep-2013	Male	40	18	Distal	11	4	15	7	0	0	No	No	Yes	No
Accell Connexus	9 Exit															
DFDBA	10	21-Oct-2013	Female	67	30	Mesial	5	7	5	7	0	0	No	No	Yes	No
Accell Connexus	11	2-May-2014	Male	54	30	Distal	5	5	9	9	0	0	No	Yes	Yes	No
DFDBA	12	24-Mar-2013	Male	41	18	Distal	8	10	11	11	0	0	Yes	No	Yes	Yes
DFDBA	13	4-Mar-2014	Female	25	18	Distal	5	8	8	8	0	-3	No	No	Yes	Yes
Accell Connexus	14 Exit															
Accell Connexus	15	12-May-2014	Female	38	27	Distal	14	11	19	15	0	0	Yes	Yes	Yes	Yes

Appendix A2: Raw data on surgical date

Treatment Group	SubjectID	Surgery Date	Surgical_ Defect Class Buccal	Surgical_ Defect Class Lingual	Surgical_ CEJ-Base Buccal	Surgical_ CEJ-Base Lingual	Surgical_ Depth Buccal	Surgical_ Depth Lingual	Surgical_ M-D Width Buccal	Surgical_ M-D Width Lingual	Surgical_ B-L Width Buccal	Surgical_B-L Width Lingual
Accell Connexus	1	17-Jan-2013	3	3	6	5	4	4	3	3	7	7
DFDBA	2	9-May-2013	3	3	13	14	10	9	2	2	9	9
Accell Connexus	3	5-Mar-2013	3	3	6	7	5	4	3	3	7	7
DFDBA	4	15-Apr-2013	1	3	10	9	7	4	4	4	9	9
Accell Connexus	5	15-Apr-2013	2	2	6	8	3	5	3	3	7	7
DFDBA	6	24-Oct-2013	3	3	6	6	5	4	5	6	13	13
DFDBA	7	15-May-2013	2	3	6	8	4	5	2	3	9	9
DFDBA	8	23-Sep-2013	3	3	11	10	9	8	4	3	9	9
Accell Connexus	9 Exit											
DFDBA	10	21-Oct-2013	3	3	5	6	3	4	1	1	6	6
Accell Connexus	11	2-May-2014	3	3	7	8	5	5	2	3	7	7
DFDBA	12	24-Mar-2014	3	3	7	9	5	7	6	6	11	11
DFDBA	13	4-Mar-2014	3	3	6	7	4	5	3	3	8	8
Accell Connexus	14 Exit											
Accell Connexus	15	12-May-2014	3	3	14	14	9	10	13	4	8	8

Appendix A3: Raw data at 6 months post-surgery

Treatment Group	SubjectID	SixMonth Date	SixMonth_ Probing Depth Buccal mm	SixMonth_ Probing Depth Lingual mm	SixMonth_ CAL Buccal	SixMonth_ CAL Lingual	SixMonth_ Recession Buccal	SixMonth_ Recession Lingual	SixMonth_ Plaque Buccal	SixMonth_ Plaque Lingual	SixMonth_ BOP Buccal	SixMonth_ BOP Lingual
Accell Connexus	1	18-Jul-2013	4	5	7	5	0	0	No	Yes	No	Yes
DFDBA	2	4-Dec-2013	4	5	8	9	0	1	No	Yes	No	Yes
Accell Connexus	3	24-Sep-2013	3	4	8	7	1	2	No	No	Yes	Yes
DFDBA	4	16-Oct-2013	2	4	3	4	1	0	No	No	No	Yes
Accell Connexus	5	18-Oct-2013	3	3	5	5	2	2	No	No	No	No
DFDBA	6	5-May-2014	4	5	8	9	0	0	No	No	No	Yes
DFDBA	7	21-Nov-2013	3	4	9	10	2	1	Yes	Yes	Yes	No
DFDBA	8	18-Mar-2014	6	4	9	7	0	-1	Yes	Yes	Yes	Yes
Accell Connexus	9 Exit											
DFDBA	10	22-Apr-2014	2	4	7	8	1	1	No	No	No	No
Accell Connexus	11	3-Dec-2014	4	4	8	9	0	0	No	No	No	No
DFDBA	12	26-Sep-2014	3	3	7	6	0	-1	No	No	No	No
DFDBA	13	4-Sep-2014	7	7	10	10	-4	-4	Yes	Yes	No	Yes
Accell Connexus	14 Exit											
Accell Connexus	15	9-Dec-2014	3	3	7	7	0	2	No	Yes	No	No

Appendix A4: Raw data at 12 months post-surgery

Treatment Group	SubjectID	TwelveMonth Date	TwelveMonth_Probing Depth Buccal mm	TwelveMonth_Probing Depth Lingual mm	TwelveMonth_CAL Buccal	TwelveMonth_CAL Lingual	TwelveMonth_Recession Buccal	TwelveMonth_Recession Lingual	TwelveMonth_Plaque Buccal	TwelveMonth_Plaque Lingual	TwelveMonth_BOP Buccal	TwelveMonth_BOP Lingual
Accell Connexus	1	16-Jan-2014	3	5	9	7	1	0	Yes	Yes	Yes	No
DFDBA	2	21-May-2014	4	3	7	8	1	2	No	No	No	Yes
Accell Connexus	3	19-Mar-2014	4	4	9	8	0	0	No	Yes	Yes	No
DFDBA	4	4-Apr-2014	3	5	9	11	1	1	No	No	Yes	Yes
Accell Connexus	5	18-Jun-2014	2	3	10	9	2	3	No	No	No	No
DFDBA	6	12-Nov-2014	3	5	6	8	0	0	No	Yes	No	Yes
DFDBA	7	28-May-2014	3	3	9	8	1	1	No	No	Yes	No
DFDBA	8	24-Sep-2014	4	2	9	7	0	0	Yes	Yes	Yes	Yes
Accell Connexus	9 Exit											
DFDBA	10	5-Nov-2014	2	4	7	9	1	0	Yes	No	Yes	No
Accell Connexus	11	14-May-2015	4	3	8	8	0	1	No	Yes	No	No
DFDBA	12	25-Mar-2015	3	3	6	7	0	0	No	No	Yes	Yes
DFDBA	13	16-Mar-2015	4	4	2	3	0	0	No	Yes	No	Yes
Accell Connexus	14 Exit											
Accell Connexus	15	13-May-2015	2	3	7	7	0	2	No	No	No	No

Appendix A5: Raw data at radiographic baseline and 6 and 12 months post-surgery

Treatment Group	Subject ID	Radio_Baseline_CEJ-Base	Radio_Baseline_CEJ-Apex	Radio_Baseline_CEJ-Alveolar	Radio_Six Month_CEJ-Base	Radio_Six Month_CEJ-Apex	Radio_Six Month_CEJ-Alveolar	Radio_Twelve Month_CEJ-Base	Radio_Twelve Month_CEJ-Apex	Radio_Twelve Month_CEJ-Alveolar
Accell Connexus	1	4.51	11.6	0.74	3.08	11.57	0.96	3	11.67	0.78
DFDBA	2	9.96	13.28	1.18	5.76		2.64	5.91		2.04
Accell Connexus	3	5.43	14.34	1.89	4.57	13.48	2.65	3.48	12.83	1.94
DFDBA	4	5.25	16.66	2.15	3.83		1.48	5.02		1.54
Accell Connexus	5	7.9	18.41	3.5	0	19.68	6.21	0	16.46	4.37
DFDBA	6	5.07	13.27	2.18	3.81	12.13	0.51	1.59	12.34	0.4
DFDBA	7	4.99	15.28	1.75	2.46	11.4	1.97	4.05	13.55	2.59
DFDBA	8	9.32	11.48	1.79	3.26	15.41	1.13	0	12.58	1.53
Accell Connexus	9 Exit									
DFDBA	10	4.81	21.89	1.47	2.75	15.72	0.72	0	15.37	0.24
Accell Connexus	11	5.69	13.41	3.6	2.8	12.16	2	2.91	12.56	1.9
DFDBA	12	6.27	14.21	1.53	3.49	13.95	1.78	2.07	13.97	1.11
DFDBA	13	3.62	15.17	0.37	1.8	15.82	0	1.11	15.01	0.28
Accell Connexus	14 Exit									
Accell Connexus	15	12.4	16.5	5.16	3.2	16.3	3.2	2.9	15.6	2.9

TreatmentGroup_num = Accell Connexus

[a]	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean	Standard Deviation	Valid N
MAX_Baseline_ProbingDepth	5.00	14.00	6.00	6.00	7.00	7.60	3.65	5
MAX_Baseline_CAL	9.00	19.00	11.00	10.00	11.00	12.00	4.00	5
MAX_Baseline_Recession	.00	1.00	.00	.00	.00	.20	.45	5
MAX_Surgical_DefectClass	2.00	3.00	3.00	3.00	3.00	2.80	.45	5
MAX_Surgical_CEJBase	6.00	14.00	8.00	7.00	8.00	8.60	3.13	5
MAX_Surgical_Depth	4.00	10.00	5.00	5.00	5.00	5.80	2.39	5
MAX_Surgical_MDWidth	3.00	13.00	3.00	3.00	3.00	5.00	4.47	5
MAX_Surgical_BLWidth	7.00	8.00	7.00	7.00	7.00	7.20	.45	5
MAX_SixMonth_ProbingDepth	3.00	5.00	4.00	3.00	4.00	3.80	.84	5
MAX_SixMonth_CAL	5.00	9.00	7.00	7.00	8.00	7.20	1.48	5
MAX_SixMonth_Recession	.00	2.00	2.00	.00	2.00	1.20	1.10	5
MAX_TwelveMonth_ProbingDepth	3.00	5.00	4.00	3.00	4.00	3.80	.84	5
MAX_TwelveMonth_CAL	7.00	10.00	9.00	8.00	9.00	8.60	1.14	5
MAX_TwelveMonth_Recession	.00	3.00	1.00	1.00	2.00	1.40	1.14	5
Change6moProbingDepth_MAX	-11.00	-1.00	-2.00	-4.00	-1.00	-3.80	4.21	5
PChange6moProbingDepth_MAX	-78.57	-16.67	-33.33	-57.14	-20.00	-41.14	26.29	5
Change12moProbingDepth_MAX	-11.00	-1.00	-2.00	-4.00	-1.00	-3.80	4.21	5
PChange12moProbingDepth_MAX	-78.57	-16.67	-33.33	-57.14	-20.00	-41.14	26.29	5
Change6moCAL_MAX	-12.00	.00	-4.00	-6.00	-2.00	-4.80	4.60	5
PChange6moCAL_MAX	-63.16	.00	-36.36	-54.55	-20.00	-34.81	25.63	5
Change12moCAL_MAX	-12.00	-1.00	-1.00	-2.00	-1.00	-3.40	4.83	5
PChange12moCAL_MAX	-63.16	-9.09	-11.11	-18.18	-10.00	-22.31	23.12	5
Change6moRecession_MAX	.00	2.00	1.00	.00	2.00	1.00	1.00	5
Change12moRecession_MAX	-1.00	3.00	1.00	1.00	2.00	1.20	1.48	5

a. TreatmentGroup_num = Accell Connexus

TreatmentGroup_num = Accell Connexus

[a]	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean	Stand Devia
Age	22.0	54.0	39.0	38.0	45.0	39.6	11.7
Baseline_ProbingDepthBuccalmm	5.0	14.0	6.0	6.0	7.0	7.6	3.6
Baseline_ProbingDepthLingualmm	4.0	11.0	5.0	5.0	6.0	6.2	2.8
Baseline_CALBuccal	9.0	19.0	11.0	10.0	11.0	12.0	4.0
Baseline_CALLingual	8.0	15.0	9.0	9.0	11.0	10.4	2.8
Baseline_RecessionBuccal	.0	.0	.0	.0	.0	.0	.0
Baseline_RecessionLingual	.0	1.0	.0	.0	.0	.2	.4
Surgical_DefectClassBuccal	2.0	3.0	3.0	3.0	3.0	2.8	.4
Surgical_DefectClassLingual	2.0	3.0	3.0	3.0	3.0	2.8	.4
Surgical_CEJBaseBuccal	6.0	14.0	6.0	6.0	7.0	7.8	3.5
Surgical_CEJBaseLingual	5.0	14.0	8.0	7.0	8.0	8.4	3.4
Surgical_DepthBuccal	3.0	9.0	5.0	4.0	5.0	5.2	2.3
Surgical_DepthLingual	4.0	10.0	5.0	4.0	5.0	5.6	2.5
Surgical_MDWidthBuccal	2.0	13.0	3.0	3.0	3.0	4.8	4.6
Surgical_MDWidthLingual	3.0	4.0	3.0	3.0	3.0	3.2	.4
Surgical_BLWidthBuccal	7.0	8.0	7.0	7.0	7.0	7.2	.4
Surgical_BLWidthLingual	7.0	8.0	7.0	7.0	7.0	7.2	.4
SixMonth_ProbingDepthBuccalmm	3.0	4.0	3.0	3.0	4.0	3.4	.5
SixMonth_ProbingDepthLingualmm	3.0	5.0	4.0	3.0	4.0	3.8	.8
SixMonth_CALBuccal	5.0	8.0	7.0	7.0	8.0	7.0	1.2
SixMonth_CALLingual	5.0	9.0	7.0	5.0	7.0	6.6	1.7
SixMonth_RecessionBuccal	.0	2.0	.0	.0	1.0	.6	.9
SixMonth_RecessionLingual	.0	2.0	2.0	.0	2.0	1.2	1.1
TwelveMonth_ProbingDepthBuccalmm	2.0	5.0	4.0	2.0	4.0	3.4	1.3
TwelveMonth_ProbingDepthLingualmm	3.0	4.0	3.0	3.0	3.0	3.2	.4
TwelveMonth_CALBuccal	7.0	10.0	9.0	8.0	9.0	8.6	1.1
TwelveMonth_CALLingual	7.0	9.0	8.0	7.0	8.0	7.8	.8
TwelveMonth_RecessionBuccal	.0	2.0	.0	.0	1.0	.6	.9
TwelveMonth_RecessionLingual	.0	3.0	1.0	.0	2.0	1.2	1.3
Radio_Baseline_CEJBase	4.51	12.40	5.69	5.43	7.90	7.19	3.17
Radio_Baseline_CEJApex	11.60	18.41	14.34	13.41	16.50	14.85	2.66
Radio_Baseline_CEJAlveolar	.74	5.16	3.50	1.89	3.60	2.98	1.70
Radio_SixMonth_CEJBase	.00	4.57	3.08	2.80	3.20	2.73	1.67
Radio_SixMonth_CEJApex	11.57	19.68	13.48	12.16	16.30	14.64	3.36
Radio_SixMonth_CEJAlveolar	.96	6.21	2.65	2.00	3.20	3.00	1.98
Radio_TwelveMonth_CEJBase	.00	3.48	2.91	2.90	3.00	2.46	1.39
Radio_TwelveMonth_CEJApex	11.67	16.46	12.83	12.56	15.60	13.82	2.08
Radio_TwelveMonth_CEJAlveolar	.78	4.37	1.94	1.90	2.90	2.38	1.34
Change6moProbingDepthBuccalmm	-11.00	-1.00	-3.00	-4.00	-2.00	-4.20	3.96
PChange6moProbingDepthBuccalmm	-78.57	-20.00	-50.00	-57.14	-33.33	-47.81	22.48
Change12moProbingDepthBuccalmm	-12.00	-1.00	-2.00	-5.00	-1.00	-4.20	4.66
PChange12moProbingDepthBuccalmm	-85.71	-16.67	-33.33	-71.43	-20.00	-45.43	31.30
Change6moProbingDepthLingualmm	-8.00	1.00	-1.00	-3.00	-1.00	-2.40	3.44
PChange6moProbingDepthLingualmm	-72.73	25.00	-20.00	-50.00	-20.00	-27.55	36.81
Change12moProbingDepthLingualmm	-8.00	-1.00	-2.00	-3.00	-1.00	-3.00	2.92
PChange12moProbingDepthLingualmm	-72.73	-20.00	-40.00	-50.00	-25.00	-41.55	21.12
Change6moCALBuccal	-12.00	-1.00	-4.00	-6.00	-2.00	-5.00	4.36
PChange6moCALBuccal	-63.16	-11.11	-36.36	-54.55	-20.00	-37.04	22.09
Change12moCALBuccal	-12.00	-1.00	-1.00	-2.00	-1.00	-3.40	4.83
PChange12moCALBuccal	-63.16	-9.09	-11.11	-18.18	-10.00	-22.31	23.12
Change6moCALLingual	-8.00	.00	-3.00	-6.00	-2.00	-3.80	3.19
PChange6moCALLingual	-54.55	.00	-37.50	-53.33	-22.22	-33.52	22.92
Change12moCALLingual	-8.00	-1.00	-1.00	-2.00	-1.00	-2.60	3.05
PChange12moCALLingual	-53.33	-11.11	-12.50	-18.18	-11.11	-21.25	18.17

Change6moRecessionBuccal	.00	2.00	.00	.00	1.00	.60	.89
Change12moRecessionBuccal	.00	2.00	.00	.00	1.00	.60	.89
Change6moRecessionLingual	.00	2.00	1.00	.00	2.00	1.00	1.00
Change12moRecessionLingual	-1.00	3.00	1.00	.00	2.00	1.00	1.58
Change6moRadio_Baseline_CEJBase	-9.20	-.86	-2.89	-7.90	-1.43	-4.46	3.84
PChange6moRadio_Baseline_CEJBase	-100.00	-15.84	-50.79	-74.19	-31.71	-54.51	33.49
Change12moRadio_Baseline_CEJBase	-9.50	-1.51	-2.78	-7.90	-1.95	-4.73	3.70
PChange12moRadio_Baseline_CEJBase	-100.00	-33.48	-48.86	-76.61	-35.91	-58.97	28.63
Change6moRadio_Baseline_CEJApex	-1.25	1.27	-.20	-.86	-.03	-.21	.97
PChange6moRadio_Baseline_CEJApex	-9.32	6.90	-1.21	-6.00	-.26	-1.98	6.17
Change12moRadio_Baseline_CEJApex	-1.95	.07	-.90	-1.51	-.85	-1.03	.76
PChange12moRadio_Baseline_CEJApex	-10.59	.60	-6.34	-10.53	-5.45	-6.46	4.60
Change6moRadio_Baseline_CEJAlveolar	-1.96	2.71	.22	-1.60	.76	.03	1.90
PChange6moRadio_Baseline_CEJAlveolar	-44.44	77.43	29.73	-37.98	40.21	12.99	52.61
Change12moRadio_Baseline_CEJAlveolar	-2.26	.87	.04	-1.70	.05	-.60	1.32
PChange12moRadio_Baseline_CEJAlveolar	-47.22	24.86	2.65	-43.80	5.41	-11.62	32.12
a. TreatmentGroup_num = Accell Connexus							

TreatmentGroup_num = DFDBA

[a]	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean	Standard Deviation	Valid N
MAX_Baseline_ProbingDepth	7.00	11.00	7.00	7.00	9.00	8.00	1.60	8
MAX_Baseline_CAL	7.00	15.00	11.00	9.50	12.50	11.00	2.56	8
MAX_Baseline_Recession	.00	.50	.00	.00	.00	.06	.18	8
MAX_Surgical_DefectClass	3.00	3.00	3.00	3.00	3.00	3.00	.00	8
MAX_Surgical_CEJBase	6.00	14.00	8.50	6.50	10.50	8.88	2.75	8
MAX_Surgical_Depth	4.00	10.00	6.00	5.00	8.00	6.50	2.14	8
MAX_Surgical_MDWidth	1.00	6.00	3.50	2.50	5.00	3.63	1.77	8
MAX_Surgical_BLWidth	6.00	13.00	9.00	8.50	10.00	9.25	2.05	8
MAX_SixMonth_ProbingDepth	3.00	7.00	4.50	4.00	5.50	4.75	1.28	8
MAX_SixMonth_CAL	4.00	10.00	9.00	7.50	9.50	8.25	1.98	8
MAX_SixMonth_Recession	-4.00	2.00	.50	.00	1.00	.13	1.81	8
MAX_TwelveMonth_ProbingDepth	3.00	5.00	4.00	3.50	4.50	4.00	.76	8
MAX_TwelveMonth_CAL	3.00	11.00	8.50	7.50	9.00	8.00	2.33	8
MAX_TwelveMonth_Recession	.00	2.00	.50	.00	1.00	.63	.74	8
Change6moProbingDepth_MAX	-7.00	-1.00	-3.00	-4.00	-2.00	-3.25	1.91	8
PChange6moProbingDepth_MAX	-70.00	-12.50	-42.86	-44.16	-28.57	-39.21	16.76	8
Change12moProbingDepth_MAX	-7.00	-2.00	-3.50	-5.50	-2.50	-4.00	2.00	8
PChange12moProbingDepth_MAX	-70.00	-28.57	-46.43	-60.39	-35.71	-47.95	15.23	8
Change6moCAL_MAX	-9.00	2.00	-2.00	-5.00	-.50	-2.75	3.58	8
PChange6moCAL_MAX	-69.23	25.00	-18.18	-38.18	-1.19	-19.92	30.02	8
Change12moCAL_MAX	-6.00	2.00	-3.00	-4.50	-2.50	-3.00	2.39	8
PChange12moCAL_MAX	-62.50	28.57	-27.27	-38.18	-20.19	-25.65	25.99	8
Change6moRecession_MAX	-4.00	2.00	.25	.00	1.00	.06	1.78	8
Change12moRecession_MAX	.00	1.50	.50	.00	1.00	.56	.62	8

a. TreatmentGroup_num = DFDBA

TreatmentGroup_num = DFDBA

[a]	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean	Stanc Devia
Age	25.0	67.0	40.5	28.5	50.0	41.3	14.4
Baseline_ProbingDepthBuccalmm	3.0	11.0	6.0	5.0	7.5	6.4	2.4
Baseline_ProbingDepthLingualmm	4.0	10.0	7.0	6.0	7.5	6.9	1.8
Baseline_CALBuccal	5.0	15.0	11.0	8.5	11.0	10.1	2.9
Baseline_CALLingual	7.0	13.0	9.0	7.5	11.5	9.5	2.3
Baseline_RecessionBuccal	.0	.0	.0	.0	.0	.0	.0
Baseline_RecessionLingual	-3.0	.5	.0	.0	.0	-.3	1.1
Surgical_DefectClassBuccal	1.0	3.0	3.0	2.5	3.0	2.6	.7
Surgical_DefectClassLingual	3.0	3.0	3.0	3.0	3.0	3.0	.0
Surgical_CEJBaseBuccal	5.0	13.0	6.5	6.0	10.5	8.0	2.9
Surgical_CEJBaseLingual	6.0	14.0	8.5	6.5	9.5	8.6	2.6
Surgical_DepthBuccal	3.0	10.0	5.0	4.0	8.0	5.9	2.5
Surgical_DepthLingual	4.0	9.0	5.0	4.0	7.5	5.8	2.0
Surgical_MDWidthBuccal	1.0	6.0	3.5	2.0	4.5	3.4	1.7
Surgical_MDWidthLingual	1.0	6.0	3.0	2.5	5.0	3.5	1.8
Surgical_BLWidthBuccal	6.0	13.0	9.0	8.5	10.0	9.3	2.1
Surgical_BLWidthLingual	6.0	13.0	9.0	8.5	10.0	9.3	2.1
SixMonth_ProbingDepthBuccalmm	2.0	7.0	3.5	2.5	5.0	3.9	1.8
SixMonth_ProbingDepthLingualmm	3.0	7.0	4.0	4.0	5.0	4.5	1.2
SixMonth_CALBuccal	3.0	10.0	8.0	7.0	9.0	7.6	2.1
SixMonth_CALLingual	4.0	10.0	8.5	6.5	9.5	7.9	2.1
SixMonth_RecessionBuccal	-4.0	2.0	.0	.0	1.0	.0	1.8
SixMonth_RecessionLingual	-4.0	1.0	.0	-1.0	1.0	-.4	1.7
TwelveMonth_ProbingDepthBuccalmm	2.0	4.0	3.0	3.0	4.0	3.3	.7
TwelveMonth_ProbingDepthLingualmm	2.0	5.0	3.5	3.0	4.5	3.6	1.1
TwelveMonth_CALBuccal	2.0	9.0	7.0	6.0	9.0	6.9	2.4
TwelveMonth_CALLingual	3.0	11.0	8.0	7.0	8.5	7.6	2.3
TwelveMonth_RecessionBuccal	.0	1.0	.5	.0	1.0	.5	.5
TwelveMonth_RecessionLingual	.0	2.0	.0	.0	1.0	.5	.8
Radio_Baseline_CEJBase	3.62	9.96	5.16	4.90	7.80	6.16	2.27
Radio_Baseline_CEJApex	11.48	21.89	14.69	13.28	15.97	15.16	3.14
Radio_Baseline_CEJAlveolar	.37	2.18	1.64	1.33	1.97	1.55	.58
Radio_SixMonth_CEJBase	1.80	5.76	3.38	2.61	3.82	3.40	1.18
Radio_SixMonth_CEJApex	11.40	15.82	14.68	12.13	15.72	14.07	1.92
Radio_SixMonth_CEJAlveolar	.00	2.64	1.31	.62	1.88	1.28	.86
Radio_TwelveMonth_CEJBase	.00	5.91	1.83	.56	4.54	2.47	2.26
Radio_TwelveMonth_CEJApex	12.34	15.37	13.76	12.58	15.01	13.80	1.24
Radio_TwelveMonth_CEJAlveolar	.24	2.59	1.32	.34	1.79	1.22	.87
Change6moProbingDepthBuccalmm	-5.00	2.00	-3.00	-4.50	-1.00	-2.50	2.45
PChange6moProbingDepthBuccalmm	-66.67	40.00	-44.16	-61.25	-16.67	-33.85	36.64
Change12moProbingDepthBuccalmm	-7.00	.00	-3.00	-4.50	-1.50	-3.13	2.23
PChange12moProbingDepthBuccalmm	-63.64	.00	-53.57	-61.25	-26.67	-43.33	23.34
Change6moProbingDepthLingualmm	-7.00	.00	-2.50	-3.00	-.50	-2.38	2.26
PChange6moProbingDepthLingualmm	-70.00	.00	-35.71	-42.86	-6.25	-29.96	24.51
Change12moProbingDepthLingualmm	-7.00	.00	-3.50	-4.00	-2.00	-3.25	2.05
PChange12moProbingDepthLingualmm	-70.00	.00	-50.00	-57.14	-35.71	-44.46	21.60
Change6moCALBuccal	-8.00	2.00	-3.00	-5.00	1.00	-2.50	3.63
PChange6moCALBuccal	-72.73	40.00	-27.27	-38.18	12.50	-17.33	36.88
Change12moCALBuccal	-6.00	2.00	-4.50	-5.50	-1.00	-3.25	2.96
PChange12moCALBuccal	-75.00	40.00	-38.18	-45.45	-9.09	-27.56	34.92
Change6moCALLingual	-9.00	2.00	-.50	-3.50	1.00	-1.63	3.70
PChange6moCALLingual	-69.23	25.00	-5.00	-31.06	13.39	-11.20	32.11
Change12moCALLingual	-5.00	2.00	-2.00	-4.00	.00	-1.88	2.42
PChange12moCALLingual	-62.50	28.57	-17.69	-34.85	.00	-17.38	27.72
Change6moRecessionBuccal	-4.00	2.00	.00	.00	1.00	.00	1.77

Change12moRecessionBuccal	.00	1.00	.50	.00	1.00	.50	.53
Change6moRecessionLingual	-1.00	1.00	.00	-1.00	.75	-.06	.86
Change12moRecessionLingual	.00	3.00	.50	.00	1.25	.81	1.07
Change6moRadio_Baseline_CEJBase	-6.06	-1.26	-2.30	-3.49	-1.62	-2.77	1.62
PChange6moRadio_Baseline_CEJBase	-65.02	-24.85	-43.58	-50.49	-34.61	-43.40	13.00
Change12moRadio_Baseline_CEJBase	-9.32	-.23	-3.77	-4.51	-1.73	-3.69	2.79
PChange12moRadio_Baseline_CEJBase	-100.00	-4.38	-67.81	-84.67	-29.75	-58.61	34.96
Change6moRadio_Baseline_CEJApex	-6.17	3.93	-.70	-3.88	.65	-1.15	3.54
PChange6moRadio_Baseline_CEJApex	-28.19	34.23	-5.21	-25.39	4.28	-4.25	22.80
Change12moRadio_Baseline_CEJApex	-6.52	1.10	-.59	-1.73	-.16	-1.41	2.67
PChange12moRadio_Baseline_CEJApex	-29.79	9.58	-4.35	-11.32	-1.05	-6.88	13.24
Change6moRadio_Baseline_CEJAlveolar	-1.67	1.46	-.52	-.71	.24	-.27	.93
PChange6moRadio_Baseline_CEJAlveolar	-100.00	123.73	-34.02	-63.81	14.46	-17.88	69.67
Change12moRadio_Baseline_CEJAlveolar	-1.78	.86	-.34	-.92	.38	-.34	.91
PChange12moRadio_Baseline_CEJAlveolar	-83.67	72.88	-25.89	-55.01	16.74	-17.39	55.07
a. TreatmentGroup_num = DFDBA							

Appendix D: Mann Whitney

Test Statistics[a]

	MAX_Baseline_ProbingDepth	MAX_Baseline_CAL	MAX_Baseline_Recession	MAX_Surgical_DefectClass	MAX_Surgical_CEJBase	MAX_Surgical_Depth	MAX_Surgical_MDWidth	MAX_Surgical_BLWidth
Mann-Whitney U	10.500	19.000	18.000	16.000	18.000	15.500	20.000	5.500
Wilcoxon W	25.500	34.000	54.000	31.000	33.000	30.500	56.000	20.500
Z	-1.465	-.151	-.465	-1.265	-.297	-.696	.000	-2.187
Asymp. Sig. (2-tailed)	.143	.880	.642	.206	.767	.486	1.000	.029
Exact Sig. [2*(1-tailed Sig.)]	.171[b]	.943[b]	.833[b]	.622[b]	.833[b]	.524[b]	1.000[b]	.030[b]
Exact Sig. (2-tailed)	.155	.937	.744	.385	.811	.550	1.000	.023
Exact Sig. (1-tailed)	.077	.469	.385	.385	.404	.290	.516	.009
Point Probability	.005	.055	.256	.385	.033	.081	.024	.002

a. Grouping Variable: TreatmentGroup_num

b. Not corrected for ties.

Test Statistics[a]

	MAX_SixMonth_ProbingDepth	MAX_SixMonth_CAL	MAX_SixMonth_Recession	MAX_TwelveMonth_ProbingDepth	MAX_TwelveMonth_CAL	MAX_TwelveMonth_Recession
Mann-Whitney U	11.000	11.000	12.500	17.000	17.500	11.500
Wilcoxon W	26.000	26.000	48.500	32.000	53.500	47.500
Z	-1.371	-1.347	-1.153	-.472	-.379	-1.321
Asymp. Sig. (2-tailed)	.170	.178	.249	.637	.705	.187
Exact Sig. [2*(1-tailed Sig.)]	.222[b]	.222[b]	.284[b]	.724[b]	.724[b]	.222[b]
Exact Sig. (2-tailed)	.236	.221	.287	.678	.726	.249
Exact Sig. (1-tailed)	.134	.120	.178	.422	.379	.140
Point Probability	.084	.042	.031	.210	.059	.085

a. Grouping Variable: TreatmentGroup_num

b. Not corrected for ties.

Test Statistics[a]

	Change6moProbingDepth_MAX	PChange6moProbingDepth_MAX	Change12moProbingDepth_MAX	PChange12moProbingDepth_MAX	Change6moCAL_MAX	PChange6moCAL_MAX	Change12moCAL_MAX	PChange12moCAL_MAX	Change6moRecession_MAX	Change12mo_MAX
Mann-Whitney U	17.000	20.000	14.000	15.500	14.500	13.500	12.500	13.000	14.000	13.000
Wilcoxon W	53.000	56.000	50.000	51.500	29.500	28.500	48.500	49.000	50.000	49.000
Z	-.447	.000	-.892	-.661	-.819	-.954	-1.112	-1.026	-.914	-1.070
Asymp. Sig. (2-tailed)	.655	1.000	.372	.508	.413	.340	.266	.305	.361	.285
Exact Sig. [2*(1-tailed Sig.)]	.724[b]	1.000[b]	.435[b]	.524[b]	.435[b]	.354[b]	.284[b]	.354[b]	.435[b]	.354[b]
Exact Sig. (2-tailed)	.714	1.000	.399	.540	.452	.370	.293	.335	.427	.324
Exact Sig. (1-tailed)	.352	.512	.193	.267	.228	.185	.152	.168	.247	.168
Point Probability	.042	.026	.017	.016	.031	.017	.030	.018	.116	.008

a. Grouping Variable: TreatmentGroup_num

b. Not corrected for ties.

Appendix E: Frequency Tables

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	6	46.2	46.2	46.2
	Male	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

Tooth

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3.0	1	7.7	7.7	7.7
	4.0	1	7.7	7.7	15.4
	18.0	4	30.8	30.8	46.2
	19.0	2	15.4	15.4	61.5
	26.0	1	7.7	7.7	69.2
	27.0	1	7.7	7.7	76.9
	30.0	2	15.4	15.4	92.3
	31.0	1	7.7	7.7	100.0
	Total	13	100.0	100.0	

Location

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Distal	10	76.9	76.9	76.9
	Mesial	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

Baseline_PlaqueBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	9	69.2	69.2	69.2
	Yes	4	30.8	30.8	100.0
	Total	13	100.0	100.0	

Baseline_PlaqueLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	9	69.2	69.2	69.2
	Yes	4	30.8	30.8	100.0
	Total	13	100.0	100.0	

Baseline_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	1	7.7	7.7	7.7
	Yes	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

Baseline_BOPLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	3	23.1	23.1	23.1
	Yes	10	76.9	76.9	100.0
	Total	13	100.0	100.0	

SixMonth_PlaqueBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	10	76.9	76.9	76.9
	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

SixMonth_PlaqueLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	7	53.8	53.8	53.8
	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

SixMonth_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	10	76.9	76.9	76.9
	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

SixMonth_BOPLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	46.2	46.2	46.2
	Yes	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

TwelveMonth_PlaqueBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	10	76.9	76.9	76.9
	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

TwelveMonth_PlaqueLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	7	53.8	53.8	53.8
	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

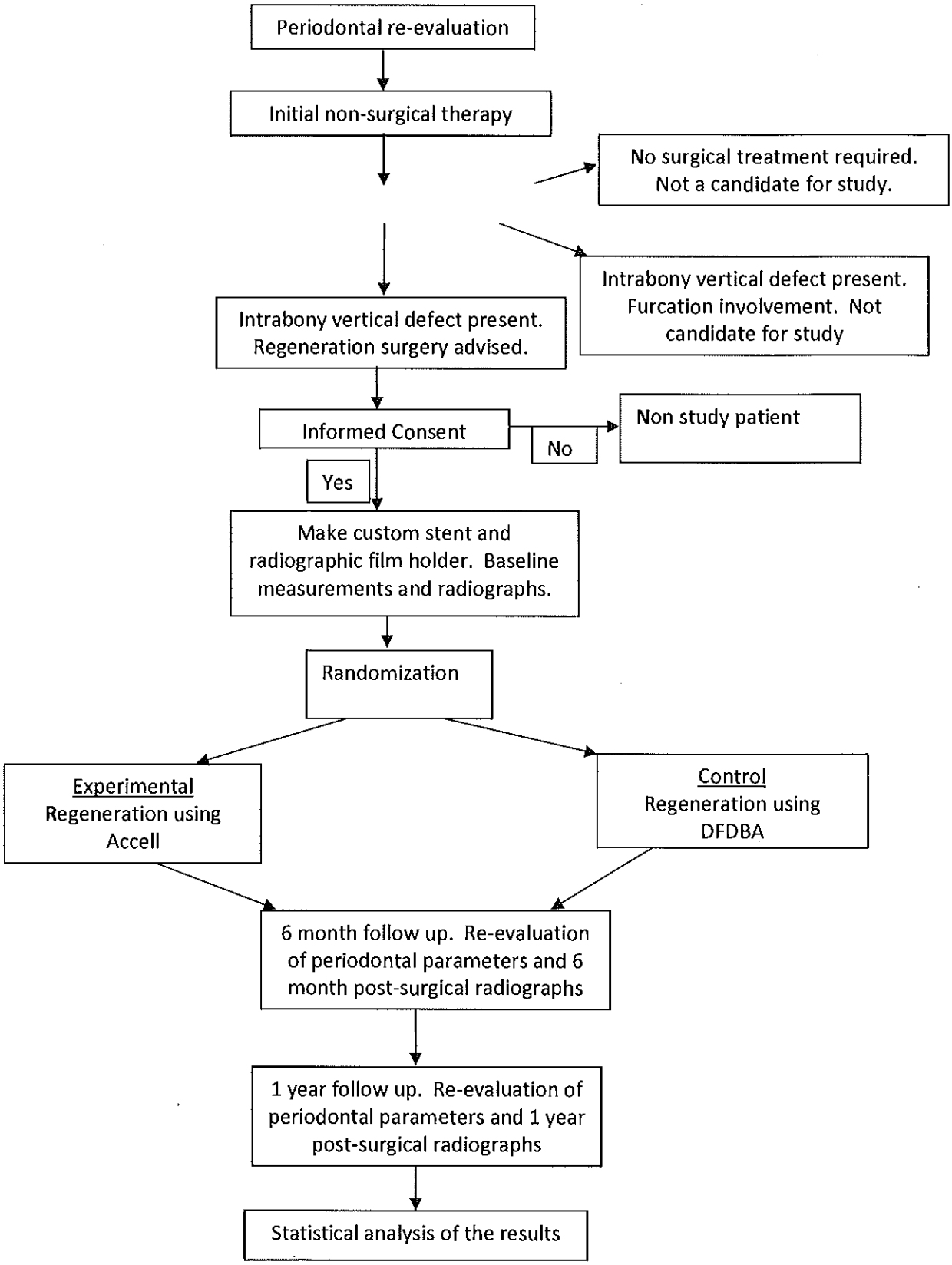
TwelveMonth_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	46.2	46.2	46.2
	Yes	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

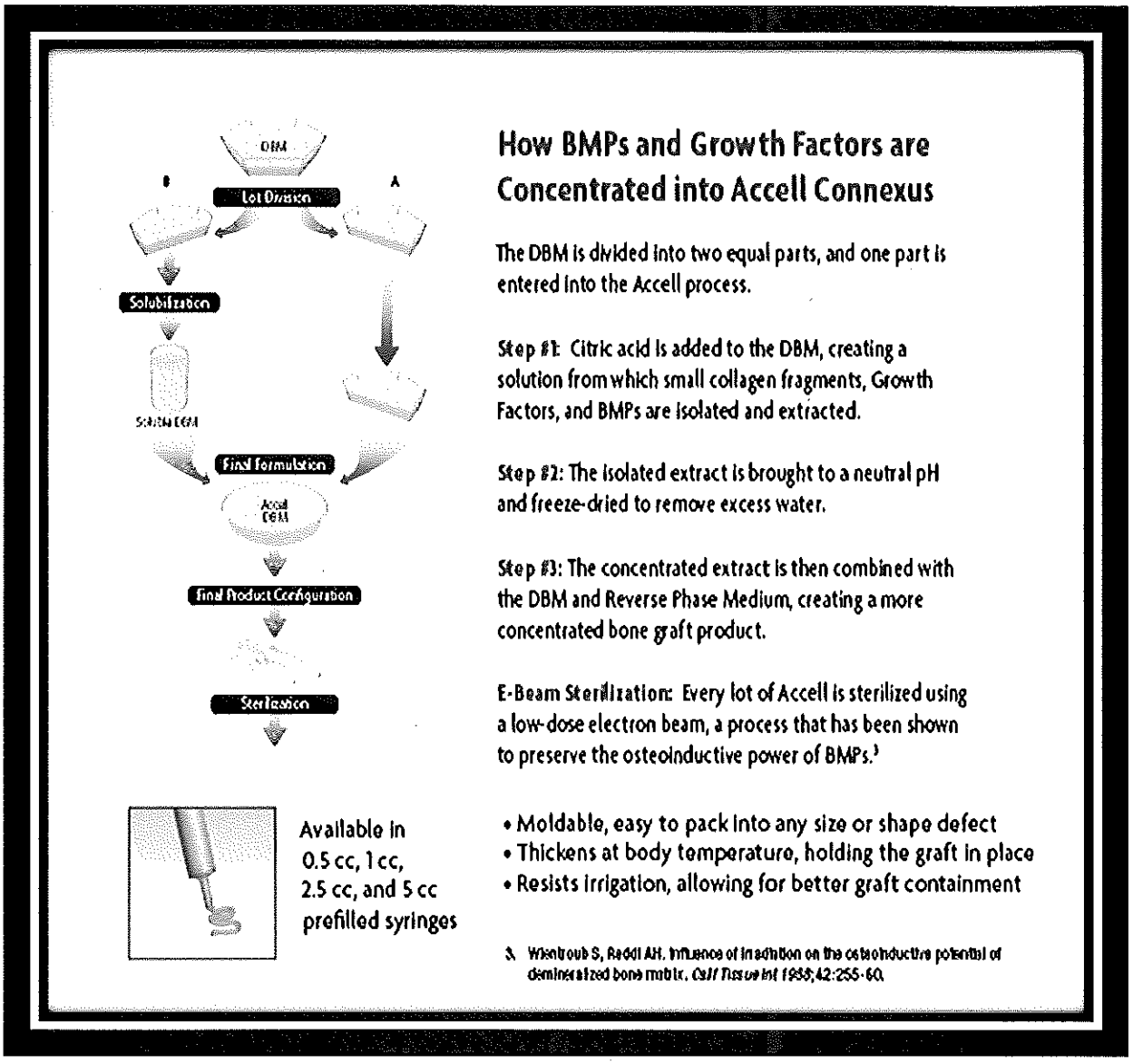
TwelveMonth_BOPLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	7	53.8	53.8	53.8
	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

Appendix F1: **FLOW DIAGRAM OF STUDY DESIGN**



Appendix F 2: Accell Brochure provided by Keystone Dental



Permission to use Accell Connexus® graphic was provided by the company, Keystone Dental. This image is published on all brochures relating to the product Accell.

Appendix G1: Inclusion/ Exclusion Check Sheet

Periodontal Regeneration of 1-, 2-, and 3-Walled Intrabony Defects Using Accell Connexus® versus Demineralized Freeze-Dried Bone Allograft: A Randomized Parallel Arm Clinical Control Trial

Inclusion/ Exclusion Check List

Subject # _____

	Inclusion	Yes(✓)/ No (X)
a.	Aged ≥18 years old	
b.	Remaining in the Capital region for at least 12 months following the surgical procedure for follow up appointments	
c.	Diagnosis of generalized or localized severe periodontitis	
d.	Radiographic evidence of a vertical intrabony defect at one or more sites with a probing depth ≥ 6 mm	
	Exclusion	
a.	Under the age of 18	
b.	Moving from the Capital region area prior to 12 months following the surgical treatment	
c.	Furcation involvement in combination with the intrabony defect determined pre-surgically	
d.	Restorations extending beyond the CEJ at the intrabony defect site	
e.	Indiscernible CEJ either clinically or radiographically	
f.	Periapical pathology, unrestored caries, defective restorations, root resorption, or vertical root fracture	
g.	Requiring restorative dental care (fillings and crown and bridge work) that cannot be completed prior to fabrication of the customized stent	
h.	Female patients who are pregnant or nursing	
i.	Currently smoke tobacco or use tobacco products. Former smokers will be excluded if they quit smoking < 6 months prior to selection in the study.	
j.	Clinically significant systemic diseases, which may affect healing (e.g. uncontrolled diabetes).	
k.	Allergic to chlorhexidine gluconate (Peridex).	
l.	Allergic to tetracycline	
m.	Poor oral hygiene unsuitable for periodontal surgery	
n.	Cannot or will not sign the informed consent form	
o.	Receiving immunosuppressive therapy such as chemotherapy and systemic corticosteroids not to include inhaled or topical steroids	
p.	Severe endocrine-induced bone diseases (e.g. hyper-thyroidism, altered parathyroid function)	
q.	Teeth with intrabony defect have mobility classified as Miller class 2 or greater	
r.	Bleeding complications (e.g. hemophilia)	
s.	On warfarin therapy	
t.	History of osteoporosis or taking bisphosphonate medications	
u.	History of radiation therapy in the head and neck area	

A no (X) response in the inclusions criteria block or a yes (✓) response in the exclusion criteria disqualifies the patient from participating in this study.

Appendix G2: Adverse Event/ Deviation Log

Periodontal Regeneration of 1-, 2-, and 3-Walled Intrabony Defects Using Accell Connexus® versus Demineralized Freeze-Dried Bone Allograft: A Randomized Parallel Arm Clinical Control Trial

Adverse Event/Deviation Log

Subject # _____

Date of AE or Deviation from Protocol: _____

1. Was this an **Adverse Event** or a **Deviation** from the protocol? *(Please circle one.)*

2. What occurred?

_____
_____
_____
_____
_____
_____

What action was taken?

_____
_____
_____
_____
_____
_____

Appendix H1: Data Collection Sheets

A master list will associate participant's name with the last 4 numbers of their social security number, telephone number and email address. Each of the following boxes (data collection sheets) will be printed on separate pieces of paper.

Periodontal Regeneration of 1-, 2-, 3-Walled Intrabony Defects Using Accell Connexus® vs DFDBA: A Randomized Parallel Arm Clinical Trial

Date _____
Subject ID # _____
Gender _____
Age _____

Clinical Measurements:										
Tooth #:										
	Probing Depth (mm)		Clinical Attachment Level (mm)		Recession (mm)		Plaque Score (+/-)		BOP (+/-)	
	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L
Baseline										

Periodontal Regeneration of 1-, 2-, 3-Walled Intrabony Defects Using Accell Connexus® vs DFDBA: A Randomized Parallel Arm Clinical Trial

Date _____
Subject ID # _____
Gender _____
Age _____

Clinical Measurements:										
Tooth #:										
	Probing Depth (mm)		Clinical Attachment Level (mm)		Recession (mm)		Plaque Score (+/-)		BOP (+/-)	
	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L
6 months										

Periodontal Regeneration of 1-, 2-, 3-Walled Intrabony Defects Using Accell Connexus® vs DFDBA: A Randomized Parallel Arm Clinical Trial

Date _____
Subject ID # _____
Gender _____
Age _____

Clinical Measurements:					
Tooth #:					
	Probing Depth (mm) M/D-B M/D-L	Clinical Attachment Level (mm) M/D-B M/D-L	Recession (mm) M/D-B M/D-L	Plaque Score (+/-) M/D-B M/D-L	BOP (+/-) M/D-B, M/D-L

Periodontal Regeneration of 1-, 2-, 3-Walled Intrabony Defects Using Accell Connexus® vs DFDBA: A Randomized Parallel Arm Clinical Trial

Date _____
Subject ID # _____
Gender _____
Age _____

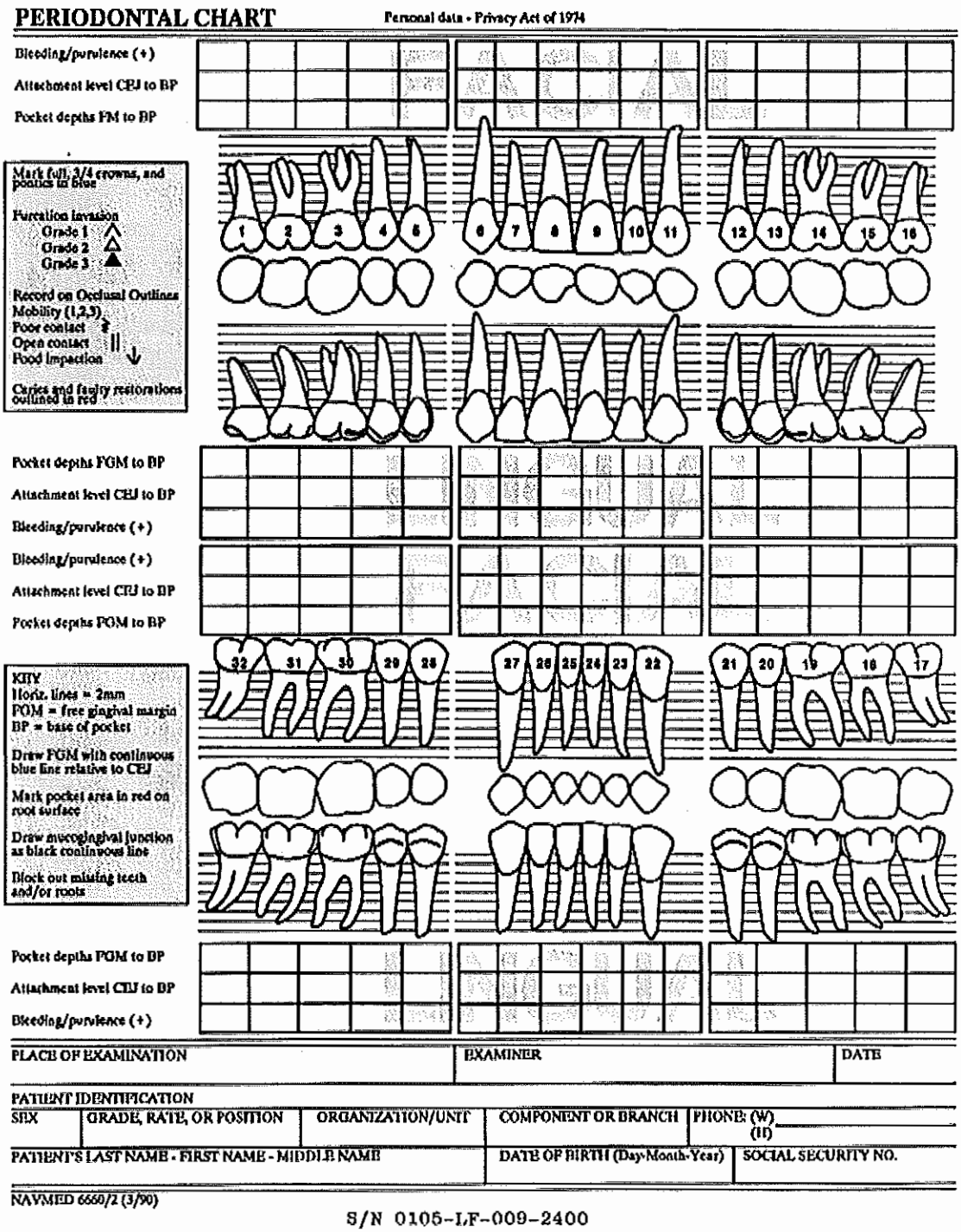
Surgical Measurements (Characterization of Defect):										
Tooth #:										
	Defect Classification (1,2,3-walled or combination) M/D-B	M/D-L	CEJ-Base of Defect (mm) M/D-B	M/D-L	Depth of Defect: Alveolar Crest-Base of Defect (mm) M/D-B	M/D-L	Width of Defect: M-D Width (mm) M/D-B	M/D-L	Width of Defect: B-L Width (mm) M/D-B	M/D-L
At Surgery										

Periodontal Regeneration of 1-, 2-, 3-Walled Intrabony Defects Using Accell Connexus® vs DFDBA: A Randomized Parallel Arm Clinical Trial

Date _____
Subject ID # _____
Gender _____
Age _____

Radiographic Measurements						
Tooth #:						
	CEJ-Base of Defect (mm)		CEJ-Apex of Tooth (mm)		CEJ-Alveolar Crest (mm)	
	M/D	M/D	M/D	M/D	M/D	M/D
Baseline						
6 months						
12 months						

Appendix H2: Comprehensive Periodontal Charting Form



PERIODONTAL CHART Personal data - Privacy Act of 1974

Bleeding/purulence (+)
Attachment level CEJ to BP
Pocket depths FM to BP

Mark full, 3/4 crowns, and pontics in blue

Furcation invasion
Grade 1
Grade 2
Grade 3

Record on Occlusal Outlines
Mobility (1,2,3)
Poor contact
Open contact
Food impaction

Caries and faulty restorations outlined in red

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

Pocket depths FGM to BP
Attachment level CEJ to BP
Bleeding/purulence (+)
Bleeding/purulence (+)
Attachment level CEJ to BP
Pocket depths FGM to BP

KEY
Horiz. lines = 2mm
FGM = free gingival margin
BP = base of pocket

Draw FGM with continuous blue line relative to CEJ

Mark pocket area in red on root surface

Draw mucogingival junction as black continuous line

Block out missing teeth and/or roots

32 31 30 29 28 27 26 25 24 23 22 21 20 19 18 17

Pocket depths FGM to BP
Attachment level CEJ to BP
Bleeding/purulence (+)

PLACE OF EXAMINATION | EXAMINER | DATE

PATIENT IDENTIFICATION

SEX | GRADE, RATE, OR POSITION | ORGANIZATION/UNIT | COMPONENT OR BRANCH | PHONE: (W) (H)

PATIENT'S LAST NAME - FIRST NAME - MIDDLE NAME | DATE OF BIRTH (Day-Month-Year) | SOCIAL SECURITY NO.

NAVMED 6660/2 (3/90)

S/N 0105-LF-009-2400

APPENDIX L: EXAMPLE OF NPDS PERIODONTICS DEPARTMENT POST-OPERATIVE INSTRUCTIONS

PERIODONTICS DEPARTMENT
NAVAL POSTGRADUATE DENTAL SCHOOL
Bethesda, Maryland

For best healing and a minimum of complications, please read and follow these instructions carefully

You may have been given one or more of these medications:

PAIN MEDICATIONS:	_____	Motrin 600 mg:	*1 tablet every 6 hours.* Do not double up on dosage.
	_____	Norco 5/325 mg:	*1 tablet every 6 hours for pain control.* It can be taken in addition to Ibuprofen. This medicine can make you drowsy. Therefore, do not drive or operate machinery while taking this drug. Additionally, do not take with alcoholic beverages; the alcohol will make you sleepier, but will not decrease your comfort.
ANTIBIOTICS:	_____	Doxycycline 100 mg:	*2 tablets the day of surgery, then 1 tablet every day for 30 days.*
	_____	Amoxicillin 500 mg:	*1 tablet four times a day for 7 to 10 days.*
	_____	Clindamycin 300 mg	*1 tablet four times a day for 7 to 10 days.*
RINSES:	_____	Peridex (Periogard	*1 bottle, rinse twice a day as directed on the bottle, starting the day following surgery.* Do not brush or floss at the surgical site unless instructed to do so.
ANTI-INFLAMMATION:	_____	Medrol Dose Pack:	Take as directed on the package, starting today. Be sure and take the full first row of tablets (first six tablets) today.

The following are a list of post-operative considerations during healing:

BLEEDING:	There may be slight bleeding from the surgical for 1-2 days after surgery. Your saliva may appear slightly reddish. This is common. If you notice an increase in bleeding please contact us.
SUTURES/STITCHES:	You may have sutures placed in your mouth. They may have to be removed in the future. Please leave the sutures alone as much as possible. Early removal or the loss of sutures may impair healing.
DRESSINGS:	There may be a gummy type of dressing or pack over the surgical area. It is there for your comfort. If it falls out before your first post-operative appointment and you are comfortable, it is fine to leave it out. If the surgical site is uncomfortable and you would like the dressing replaced please contact me.
DIET:	It is very important to maintain a soft diet for at least a week. Chew as much as possible on the side opposite the surgery. This is not the time to start a diet. Please maintain your caloric and fluid intake as at pre-surgical levels. You will not heal well if you are dehydrated or undernourished. Please do not drink using a straw.
ORAL HYGIENE:	It is very important not to brush or floss the surgical site until given express instructions. Normal brushing and flossing procedures can traumatize the tissue and impair healing. You may brush and floss those areas not affected by the surgery. To keep bacteria under control a prescription mouth rinse has been written for you. Initially, use the mouthwash as a rinse. Later you may be instructed to use a cotton-tipped applicator, dipped in the mouthwash, to swab along the gum line of the surgery site. Use a capful (15ml) of the mouthwash twice a day, morning and bedtime, after brushing/flossing your non-surgically treated teeth. You may notice a mild tooth staining as a result of the mouthwash. This is not permanent; the stain will be removed with scaling/polishing at your follow-up appointments. Please do not use a Water-Pik or other irrigator unless instructed to do so.
PHYSICAL ACTIVITY:	Avoid strenuous physical activity (to include running and heavy lifting) for 72 hours. Additionally, no vigorous spitting, rinsing, or spitting (yelling). Forceful movements at the site of surgery will negatively affect healing.
SWELLING:	You may experience some swelling. This is common and usually peaks at 2-3 days after surgery. Thereafter you should expect to see a return to normal. To decrease swelling you can apply ice to the site for the first 3-4 hours after surgery. Please call if the swelling appears to increase after the third day, or if you are concerned.
SMOKING	Smoking is deleterious to healing. We advise you to stop smoking for as long as possible after surgery. Stopping smoking will improve potential healing and also improve your overall periodontal health.
FOR SINUS LIFT SURGE PROCEDURES	You may also have received nasal decongestant tablets and spray. Please use these medications as directed on the package. In addition, avoid blowing your nose. If you need to sneeze, please sneeze with your mouth open. Please inform your doctor if you develop sinus congestion that is not minimized with your medications or if you notice any bleeding or discharge from your nose.

If you have any problems or questions, please do not hesitate to call me at 301-295-0077. If there is an emergency you may page your doctor through an automated system. Instructions will be given after dialing 1-800-759-8888. The PIN# for your doctor is_____

Your follow up appointment is scheduled for: _____ _____

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